INVENTOR SEARCH

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=> d his l101

     (FILE 'HCAPLUS' ENTERED AT 11:20:11 ON 27 JUL 2007)
L101          26 S L100 AND L50

=> d que l101
L48               QUE  ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
                  MY<2003 OR REVIEW/DT
L50               QUE  ABB=ON  PLU=ON  IMMUNOSUPPRES? OR IMMUNOREG? OR IM
                  MUN?(A)(SUPPRESS? OR REG?)
L97         1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
                  A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
                  AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
                  "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
                  "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98               QUE  ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99          714 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L48
L100         228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99 AND L98
L101          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L50


=> d his l131

     (FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 12:40:59 ON 27
     JUL 2007)
L131           6 S L130 AND (L50 OR L59)
                  SAV L131 JEA176MULTIN/A

     FILE 'STNGUIDE' ENTERED AT 12:44:10 ON 27 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 12:45:23 ON 27 JUL 2007
                  SAV L101 JEA176HCPIN/A

     FILE 'STNGUIDE' ENTERED AT 12:46:17 ON 27 JUL 2007

=> d que l131
L48               QUE  ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
                  MY<2003 OR REVIEW/DT
L50               QUE  ABB=ON  PLU=ON  IMMUNOSUPPRES? OR IMMUNOREG? OR IM
                  MUN?(A)(SUPPRESS? OR REG?)
L59               QUE  ABB=ON  PLU=ON  EDG1(A)S1P?
L97         1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
                  A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
                  AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
                  "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
                  "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98               QUE  ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L128          608 SEA L97
L129          277 SEA L128 AND L98
L130          143 SEA L129 AND L48
L131            6 SEA L130 AND (L50 OR L59)


=> dup rem l101 l131
FILE 'HCAPLUS' ENTERED AT 12:49:36 ON 27 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 12:49:36 ON 27 JUL 2007

FILE 'BIOSIS' ENTERED AT 12:49:36 ON 27 JUL 2007
Copyright (c) 2007 The Thomson Corporation
PROCESSING COMPLETED FOR L101
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PROCESSING COMPLETED FOR L131
L132          29 DUP REM L101 L131 (3 DUPLICATES REMOVED)
                 ANSWERS '1-26' FROM FILE HCAPLUS
                 ANSWERS '27-29' FROM FILE BIOSIS
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INVENTOR SEARCH RESULTS

=> d l132 1-29 ibib ed ab

L132 ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:301209 HCAPLUS Full-text
DOCUMENT NUMBER: 137:241872
TITLE: Alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists
AUTHOR(S): Mandala, Suzanne; Hajdu, Richard; Bergstrom, James; Quackenbush, Elizabeth; Xie, Jenny; Milligan, James; Thornton, Rosemary; Shei, Gan-Ju; Card, Deborah; Keohane, Carolann; Rosenbach, Mark; Hale, Jeffrey; Lynch, Christopher L.; Rupprecht, Kathleen; Parsons, William; Rosen, Hugh
CORPORATE SOURCE: Departments of Immunology and Rheumatology, Merck Res. Laboratories, Rahway, NJ, 07065, USA
SOURCE: Science (Washington, DC, United States) (2002), 296(5566), 346-349
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Apr 2002
AB Blood lymphocyte nos., essential for the development of efficient immune responses, are maintained by recirculation through secondary Lymphoid organs. We show that lymphocyte trafficking is altered by the lysophospholipid sphingosine-1-phosphate (S1P) and by a phosphoryl metabolite of the immunosuppressive agent FTY720. Both species were high-affinity agonists of at least four of the five S1P receptors. These agonists produce lymphopenia in blood and thoracic duct lymph by sequestration of lymphocytes in lymph nodes, but not spleen. S1P receptor agonists induced emptying of lymphoid sinuses by retention of lymphocytes on the abluminal side of sinus-lining endothelium and inhibition of egress into lymph. Inhibition of lymphocyte recirculation by activation of S1P receptors may result in therapeutically useful immunosuppression.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2000:618629 HCAPLUS Full-text
DOCUMENT NUMBER: 133:275898
TITLE: Efficacy of the echinocandin caspofungin against disseminated aspergillosis and candidiasis in cyclophosphamide-induced immunosuppressed mice
AUTHOR(S): Abruzzo, George K.; Gill, Charles J.; Flattery, Amy M.; Kong, Li; Leighton, Claire; Smith, Jeffrey G.; Pikounis, V. Bill; Bartizal, Ken; Rosen, Hugh
CORPORATE SOURCE: Infectious Diseases, Merck Research Laboratories, Rahway, NJ, 07065-0900, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(9), 2310-2318
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Sep 2000
AB The in vivo efficacy of the echinocandin antifungal caspofungin acetate (caspofungin; MK-0991) was evaluated in models of disseminated aspergillosis and candidiasis in mice with cyclophosphamide (CY)-induced immunosuppression. Caspofungin is a 1,3-β-D-glucan synthesis inhibitor efficacious against a number of clin. relevant fungi including

Aspergillus and Candida species. Models of CY-induced transient or chronic leukopenia were used with once daily administration of therapy initiated 24 h after microbial challenge. Caspofungin was effective in treating disseminated aspergillosis in mice that were transiently leukopenic (significant prolongation of survival at doses of ≥0.125 mg/kg of body weight and a 50% protective dose [PD50] of 0.245 mg/kg/day at 28 days after challenge) or chronically leukopenic (50 to 100% survival at doses of ≥0.5 mg/kg and PD50s ranging from 0.173 to 0.400 mg/kg/day). Caspofungin was effective in the treatment and sterilization of Candida infections in mice with transient leukopenia with a 99% ED based on reduction in log10 CFU of Candida albicans/g of kidneys of 0.119 mg/kg and 80 to 100% of the caspofungin-treated mice having sterile kidneys at caspofungin doses from 0.25 to 2.0 mg/kg. In Candida-infected mice with chronic leukopenia, caspofungin was effective at all dose levels tested (0.25 to 1.0 mg/kg), with the log10 CFU of C. albicans/g of kidneys of caspofungin-treated mice being significantly lower (>99% reduction) than that of sham-treated mice from day 4 to day 28 after challenge. Also, 70 to 100% of the caspofungin-treated, chronic leukopenic mice had sterile kidneys at caspofungin doses of 0.5 to 1.0 mg/kg from day 8 to 28 after challenge. Sterilization of Candida infections by caspofungin in the absence of host leukocytes provides compelling in vivo evidence for fungicidal activity against C. albicans. Further human clin. trials with caspofungin against serious fungal infections are in progress.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:566538 HCAPLUS Full-text
DOCUMENT NUMBER: 141:123484
TITLE: Preparation of 1-(amino)indanes and (1,2-dihydro-3-amino)-benzofurans, benzothiophenes and indoles as EDG receptor agonists
INVENTOR(S): Doherty, George A.; Hale, Jeffrey J.; Mills, Sander G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004058149 | A2 | 20040715 | WO 2003-US40129 | 2003 1216 |
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| WO 2004058149 | A3 | 20040916 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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| CA 2509218 | A1 | 20040715 | CA 2003-2509218 | 2003 1216 |
| | | | <-- | |
| AU 2003297232 | A1 | 20040722 | AU 2003-297232 | |

2003
1216
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EP 1581509 A2 20051005 EP 2003-814075
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JP 2006511579 T 20060406 JP 2004-563642
2003
1216
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US 2006161005 A1 20060720 US 2005-536730
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US 7220734 B2 20070522
PRIORITY APPLN. INFO.: US 2002-435381P P
2002
1220
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WO 2003-US40129 W
2003
1216

OTHER SOURCE(S): MARPAT 141:123484
ED Entered STN: 15 Jul 2004
AB Compds. of formula I [G = C(R4)2, O, S, SO, SO2; X = Ph, alkyl, etc.; Y = (C(R4))p; Z = alkyl, heterocyclo, etc.; A = CO2H, PO3H2, SO3H, tetrazolyl, etc.; each R1 = H, halo, OH, alkyl, alkoxy; R2 = H, halo, OH, alkyl, alkoxy; R3 =H, alkyl; R2R3 = (substituted) alkylene; R4 = H, alkyl; R5 = halo, alkyl, alkoxy; n = 0-1; p = 1-3] are prepared as EDG receptor agonists. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, II was prepared from azetidine-3-carboxylic acid and the prepared indanone derivative The prepared compds. had > 100-fold selectivity of EDG1 over EDG3.

L132 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:412748 HCAPLUS Full-text
DOCUMENT NUMBER: 140:423677
TITLE: Preparation of 3-(tetrahydropyranylamino)cyclo pentanecarboxylic acid N-benzylamide derivatives and related compounds as modulators of chemokine receptor activity
INVENTOR(S): Butora, Gabor; Mills, Sander G.; Pasternak, Alexander; Shankaran, Kothandaraman; Yang, Lihu; Zhou, Changyou; Goble, Stephen D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041161 | A2 | 20040521 | WO 2003-US33972 | 2003 1024 |
| | | | <-- | |
| WO 2004041161 | A3 | 20050324 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| CA 2502174 | A1 | 20040521 | CA 2003-2502174 | 2003 1024 |
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| AU 2003286701 | A1 | 20040607 | AU 2003-286701 | 2003 1024 |
| | | | <-- | |
| EP 1558243 | A2 | 20050803 | EP 2003-777911 | 2003 1024 |
| | | | <-- | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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|---|---|---|---|---|
| JP 2006514003 | T | 20060427 | JP 2004-550126 | 2003 1024 |
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| US 2006116421 | A1 | 20060601 | US 2005-533326 | 2005 0502 |
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| PRIORITY APPLN. INFO.: | | | US 2002-422451P P | 2002 1030 |
| | | | <-- | |
| | | | WO 2003-US33972 W | 2003 1024 |

OTHER SOURCE(S): MARPAT 140:423677

ED Entered STN: 21 May 2004

AB The title compds. (I) [wherein: X = O, NR20, S, SO, SO2, CR21R22, NSO2R20, NCOR20, NCO2R20, CR21CO2R20, CR21OCOR20, CO, OC(Me)2O (where R20 = H, C1-6 alkyl, benzyl, Ph, C3-6 cycloalkyl, etc.; R21, R22 = H, HO, C1-6 alkyl, C1-6 alkoxy, benzyl, Ph, C3-6 cycloalkyl, etc.); R1 = C1-6 alkyl, C1-6 alkoxy-C0-6 alkyl, C1-6 alkyl-S(O)0-2-C0-6-alkyl, N-(un)substituted C1-6 alkylaminosulfonyl-C0-6alkyl, -(C0-6 alkyl)(C3-7 cycloalkyl)(C0-6 alkyl), HO, CO2R20, heterocyclyl, cyano, NR20R26, NR26SO2R20, NR26COR21, OCOR20, Ph (where R26 = H, C1-6 alkyl, benzyl, Ph, etc.); R2, R4, R6 = H, C1-6 alkyl, CF3, CF3O, Cl, Br, Ph; R3 = H, HO, halo, C1-6 alkyl, C1-6 alkoxy, , NR20R21, NR20CO2R21, NR20CONR20OR21, NR20SO2NR20R21, NR20SO2R21, heterocyclyl, cyano, CONR20R21, CO2R20, NO2, SR20, SOR20, SO2R20, SO2NR20R21: R5 = C1-6 alkyl substituted with 1-6 F and optionally substituted with HO, C1-6 alkoxy or CO-C1-6 alkyl each substituted with 1-6 fluoro, C1-6 alkylthio, pyridyl, F, Cl, Br, Ph; R7 = H, C1-6 alkyl, CF3; R8, R9, R10 = H, (un)substituted C1-6 alkyl; or R7 and R8 or R8 and R9 may be joined together to form a ring; R11 = H, C1-6 alkyl, CF3; R27, R28 = oxo, H, Ph, (un)substituted C1-6 alkyl; R29, R30, R31 = H, Me, HO, CF3, MeO, CF3O; or R29 and R9 are connected by a C1-3alkyl bridge; m, n = 0-2; the dashed line = a single or a double bond] and pharmaceutically acceptable salts thereof and individual diastereomers thereof are prepared These compds. are useful as modulators of the chemokine receptor CCR-2 for (a) treating, ameliorating or controlling or reducing the risk of an inflammatory or immunoregulatory disorder or disease or (b) treating, ameliorating or controlling rheumatoid arthritis (no data). Thus, reductive amination of N-[3,5-bis(trifluoromethyl)benzyl]-3-oxo-1-isopropylcyclopentane-1- carboxamide with 4-

aminotetrahydro-4H-pyran hydrochloride using triacetoxyborohydride in the presence of diisopropylethylamine in CH2Cl2 at room temperature overnight gave 46% N-[3,5-bis(trifluoromethyl)benzyl]-3-(tetrahydro-4H-pyran-4-ylamino)-oxo- 1-isopropylcyclopentane-1-carboxamide (II).

L132 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719274 HCAPLUS Full-text
DOCUMENT NUMBER: 139:246116
TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists
INVENTOR(S): Doherty, George A.; Hale, Jeffrey J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003074008 | A2 | 20030912 | WO 2003-US7262 | 2003 0225 |
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| WO 2003074008 | A3 | 20040226 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2477449 | A1 | 20030912 | CA 2003-2477449 | 2003 0225 |
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| AU 2003218056 | A1 | 20030916 | AU 2003-218056 | 2003 0225 |
| | | | <-- | |
| EP 1482896 | A2 | 20041208 | EP 2003-714037 | 2003 0225 |
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| US 2005107345 | A1 | 20050519 | US 2003-505268 | 2003 0225 |
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| JP 2005531508 | T | 20051020 | JP 2003-572530 | 2003 0225 |
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| PRIORITY APPLN. INFO.: | | | US 2002-360605P P | 2002 0301 |

<--
WO 2003-US7262 W
2003
0225

OTHER SOURCE(S): MARPAT 139:246116
ED Entered STN: 14 Sep 2003
AB The present invention encompasses title compds., A-X[CR1R2]mCHNH2[CR3R4]pC(R9)3 (m = 1-4; p = 9-20; X = bond, O, NH, S(O)k, k = 0-2; A = CO2H, PO3H2, PO2H2, SO3H, five membered nitrogen containing heterocyclyl, etc.; two R1 or R3 groups on adjacent carbon may be joined together to form a double bond; R2, R3, R4 = H, halo, OH, CO2H, C1-4 alkyl, alkoxy, alkylthio, aryl, etc.; R1-R4 = residing on the same carbon optionally joined together to form a carbonyl group, etc.; R9 = H, halo, OH, C1-4 alkoxy, alkylthio, C3-7 cycloalkyl, etc.); as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, preparation of (+/-)-2-amino-4-(4-(octylphenyl))butanol, O-phosphate was described in five steps starting from di-Et 2-acetamido-2-(2-(4- octylphenyl)ethyl)propanedioate.

L132 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719253 HCAPLUS Full-text
DOCUMENT NUMBER: 139:245479
TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists
INVENTOR(S): Budhu, Richard J.; Doherty, George A. ; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Neway, William E., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003073986 | A2 | 20030912 | WO 2003-US5947 | 2003 0227 |
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| WO 2003073986 | A3 | 20040527 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2477423 | A1 | 20030912 | CA 2003-2477423 | 2003 0227 |
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| AU 2003217764 | A1 | 20030916 | AU 2003-217764 | 2003 0227 |
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| EP 1482895 | A2 | 20041208 | EP 2003-713727 | |

2003
0227

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005531506 T 20051020 JP 2003-572508

2003
0227

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US 2006089334 A1 20060427 US 2004-505257

2004
0819

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PRIORITY APPLN. INFO.: US 2002-360663P P

2002
0301

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WO 2003-US5947 W

2003
0227

OTHER SOURCE(S): MARPAT 139:245479
ED Entered STN: 14 Sep 2003
AB AX(CR1R2)mCH(NH2)(CR3R4)nArBC [A = CO2H, P(O)(OH)2, PH(O)(OH),SO3H, P(O)R5OH, 5-membered N heterocycle; X = bond, O, NH, S, S, S(O), SO2; R1-R4 = H, halogen, OH, CO2H, (un)substituted alkyl, alkoxy, alkylthio, aryl; R1R2, R3R4 = O; m = 1-4; n = 0-4; R5 = (un)substituted alkyl, aryl; Ar = Ph, naphthyl; C = (un)substituted alkyl, alkoxy, acyl, hydroxyalkyl, Ph, heterocyclic, bond; when C = bond, B = (un)substituted Ph, alkyl, alkenyl, alkynyl, OH, SH, acyl, CONH2, NH2; when C = Ph, heterocyclic, B = (un)substituted alkyl, alkoxy, acyl, CO, CH(OH), C6H4, heterocyclic; when C = alkyl, alkoxy, acyl, B = (un)substituted C6H4, heterocyclic] were prepared for use as EDG receptor antagonists useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 4-Me(CH2)7C6H4CH2CH2C(NHAc)(CO2Et)2 was hydrolyzed and decarboxylated to 4-Me(CH2)7C6H4CH2CH2CH(NH2)CO2H which was N-benzyloxycarbonylated, reduced to 4-Me(CH2)7C6H4CH2CH2CH(NHCbz)CH2OH, phosphorylated (MeCH)2NP(OCH2Ph)2, and deblocked to give 4- Me(CH2)7C6H4CH2CH2CH(NH2)CH2OP(O)(OH)2.

L132 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:591193 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149520
TITLE: Preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists
INVENTOR(S): Bugianesi, Robert L.; Doherty, George A.; Gentry, Amy; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Neway, William E., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2003062252 | A1 | 20030731 | WO 2003-US1196 | 2003 0115 |

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     CA 2472715          A1    20030731    CA 2003-2472715
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     EP 1470137          A1    20041027    EP 2003-705779
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     JP 2005515259       T     20050526    JP 2003-562129
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     US 2005033055       A1    20050210    US 2004-500895
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PRIORITY APPLN. INFO.:                     US 2002-350000P     P
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                                           WO 2003-US1196      W
                                                          2003
                                                          0115

OTHER SOURCE(S):         MARPAT 139:149520
ED   Entered STN:  01 Aug 2003
AB   Title compds. I [Ar = (un)substituted Ph, naphthyl; A = CO2H, P(O)(OH)2, P(O)OH, SO3H,
     1H-tetrazol-5-yl; R1, R2 = H, halogen, OH, CO2H, (un)substituted alkyl; R3 = H,
     (un)substituted alkyl; m, n = 0, 1] were prepared for use as Edg receptor agonists,
     useful for treating immune mediated diseases and conditions, such as bone marrow, organ
     and tissue transplant rejection (no data).  Thus, 3-pyrrolidinol was converted to di-Et
     3-hydroxypyrrolidin-3- ylphosphonate and treated with 4-nonylbenzaldehyde, followed by
     ester hydrolysis to give 1-(4-nonylbenzyl)-3-hydroxypyrrolidine-3- phosphonic acid.
REFERENCE COUNT:         1     THERE ARE 1 CITED REFERENCES AVAILABLE
                               FOR THIS RECORD. ALL CITATIONS AVAILABLE
                               IN THE RE FORMAT

L132 ANSWER 8 OF 29  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2003:591190  HCAPLUS  Full-text
DOCUMENT NUMBER:         139:149756
TITLE:                   Preparation of N-(benzyl)aminoalkylcarboxylate
                         s, phosphinates, phosphonates and tetrazoles
                         as EDG receptor agonists
INVENTOR(S):             Doherty, George A.; Li, Chen
                         ; Hale, Jeffrey J.; Mills,
                         Sander G.
PATENT ASSIGNEE(S):      Merck & Co., Inc., USA
SOURCE:                  PCT Int. Appl., 152 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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|---|---|---|---|
| WO 2003062248 | A2 | 20030731 | WO 2003-US1059 |
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| WO 2003062248 | A3 | 20060302 | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2472713 | A1 | 20030731 | CA 2003-2472713 |
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| JP 2005527494 | T | 20050915 | JP 2003-562125 |
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| EP 1575964 | A2 | 20050921 | EP 2003-702110 |
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| US 2005020837 | A1 | 20050127 | US 2004-500811 |
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| | | | 0707 |
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| PRIORITY APPLN. INFO.: | | | US 2002-349995P P |
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| | | | 0118 |
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| | | | WO 2003-US1059 W |
| | | | 2003 |
| | | | 0114 |

OTHER SOURCE(S): MARPAT 139:149756
ED Entered STN: 01 Aug 2003
AB The present invention encompasses preparation of compds., A(CRlR2)nNHCHR3Ar{(R4)0-4}BC (Ar = Ph, naphthyl, etc.; A = CO2H, lH-tetrazol-5-yl, PO3H2, PO2H2, SO3H, PO(R5)OH, R5 = Cl-4 alkyl, hydroxyCl-4alkyl, Ph, COCl-3alkoxy, CH(OH)Ph, etc.; n = 2-4; R1, R2 = independently selected from H, halo, OH, CO2H, C1-6 alkyl, Ph, etc.; R3 = H, Cl-4 alkyl, etc.; R4 = CO2H, C1-4 alkyl, sulfonylalkyl, alkoxy, alkoxycyclopropyl, aryl, aryloxy, etc.; C = Cl-8 alkyl, C1-8 alkoxy, heterocyclyl, etc.; B = (un)substituted Ph, (un)substituted C5-16 alkyl, (un)substituted C5-16 alkenyl, (un)substituted C5-16 alkynyl, etc.), as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical comps. and methods of use are included. Thus, reaction of 3-aminopropylphosphonic acid with 4-(decyloxy)benzaldehyde in presence of Bu4NOH and sodium cyanoborohydride in MeOH for 1h at 50° gave title compound, N-((4-decyloxy)benzyl)-3-aminopropylphosphonic acid.

L132 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:590932 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149413
TITLE: Selective S1P1/Edg1 receptor agonists

INVENTOR(S): Doherty, George A.; Forrest, Michael J.; Hajdu, Richard; Hale, Jeffrey J.; Li, Zhen; Mandala, Suzanne M.; Mills, Sander G.; Rosen, Hugh; Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003061567 | A2 | 20030731 | WO 2003-US1120 | 2003 0114 |
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| WO 2003061567 | A3 | 20031224 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004058894 | A1 | 20040325 | US 2003-339380 | 2003 0109 |
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| CA 2472680 | A1 | 20030731 | CA 2003-2472680 | 2003 0114 |
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| EP 1469863 | A2 | 20041027 | EP 2003-731917 | 2003 0114 |
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| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| AU 2003216054 | B2 | 20070104 | AU 2003-216054 | 2003 0114 |
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| US 2005070506 | A1 | 20050331 | US 2004-501176 | 2004 0712 |
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| PRIORITY APPLN. INFO.: | | | US 2002-349991P P | 2002 0118 |
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| | | | US 2002-362566P P | 2002 0307 |
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| | | | US 2002-382933P P | 2002 |

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WO 2003-US1120 W

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ED Entered STN: 01 Aug 2003

AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4- Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.

L132 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:171909 HCAPLUS Full-text
DOCUMENT NUMBER: 136:216887
TITLE: Preparation of phosphate derivatives as immunosuppressants
INVENTOR(S): Mandala, Suzanne; Bergstrom, James; Hajdu, Richard; Rosen, Hugh; Parsons, William H.; Card, Deborah J.; Maccoss, Malcolm
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002018395 | A1 | 20020307 | WO 2001-US26789 | 2001 0828 |

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| CA 2421893 | A1 | 20020307 | CA 2001-2421893 | 2001 0828 |

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| AU 2001085331 | A5 | 20020313 | AU 2001-85331 | 2001 0828 |

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| EP 1315735 | A1 | 20030604 | EP 2001-964485 | 2001 0828 |

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

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US 2002091105 A1 20020711 US 2001-942411
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US 6437165 B2 20020820
PRIORITY APPLN. INFO.: US 2000-229438P P
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WO 2001-US26789 W
2001
0828
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OTHER SOURCE(S): MARPAT 136:216887
ED Entered STN: 08 Mar 2002
AB Immunoregulatory compds. [I; wherein: X = O, S, NR1, (CH2)1-2, optionally substituted with 1-4 halo groups (R1 = H, (C1-C4)alkyl, (C1-C4)haloalkyl); R1a = H, OH, (C1-C4)alkyl, (C1- C4)alkyloxy, the alkyl and alkyloxy portions being optionally substituted with 1-3 halo groups; R1b = H, OH, (C1-C4)alkyl, (C1-C4)haloalkyl; R2 = H, (C1-C4)alkyl, (C1-C4)haloalkyl; and R3 = H, OH, halo, (C1-C4)alkyloxy, (C1-C4)haloalkyloxy], as well as the pharmaceutically acceptable salts and hydrates thereof, are disclosed. Thus, a multistep preparation of 3-amino-3-hydroxymethyl-5-(4-octylphenyl)pentylphosphonic acid is described. The compds. are useful as immunosuppressants, particularly in the treatment of bone marrow and organ transplant rejection. Pharmaceutical compns. and methods of use are included.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:12274 HCAPLUS Full-text
DOCUMENT NUMBER: 134:86272
TITLE: Preparation of pyrimidine derivatives as Src-family protein tyrosine kinase inhibitor compounds
INVENTOR(S): Hunt, Julianne A.; Mills, Sander G.; Sinclair, Peter J.; Zaller, Dennis M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2001000214 | A1 | 20010104 | WO 2000-US17472 | 2000 0626 |
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| CA 2376951 | A1 | 20010104 | CA 2000-2376951 | 2000 0626 |
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| US 6316444 | B1 | 20011113 | US 2000-603699 | 2000 0626 |
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| EP 1194152 | A1 | 20020410 | EP 2000-944858 | 2000 0626 |
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| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2003503354 | T | 20030128 | JP 2001-505923 | 2000 0626 |
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| PRIORITY APPLN. INFO.: | | | US 1999-141597P | P 1999 0630 |
| | | | <-- | |
| | | | WO 2000-US17472 | W 2000 0626 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 134:86272
ED Entered STN: 05 Jan 2001
AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-associated disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, alkoxycarbonylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered aromatic ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, Cl-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl (Ph or naphthyl unsubstituted or substituted with 1-3 substituents), or R3 and R5 taken together can represent :O. R4 = H, Cl-C6-alkyl, Cl-C6-alkoxyl, or R4 and X can join together to form a 5- or 6-membered ring with substituted methylene or ethylene. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5 = N, CH. R7 = H, alkyl, alkoxy, amino. X = O, S, SO, SO2, imino. Z = C:O, SO2, substituted P(:O)(OH) or a single bond. 44 Example prepns. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:12273 HCAPLUS Full-text
DOCUMENT NUMBER: 134:86271
TITLE: Preparation of pyrimidine derivatives as Src-family protein tyrosine kinase inhibitor compounds
INVENTOR(S): Armstrong, Helen M.; Beresis, Richard; Goulet, Joung L.; Holmes, Mark A.; Hong, Xingfang; Mills, Sander G.; Parsons, William H.; Sinclair, Peter J.; Steiner, Mark G.; Wong, Frederick; Zaller, Dennis M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 470 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001000213 | A1 | 20010104 | WO 2000-US17443 | 2000 0626 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2383546 | A1 | 20010104 | CA 2000-2383546 | 2000 0626 |
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| EP 1206265 | A1 | 20020522 | EP 2000-941701 | 2000 0626 |
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| EP 1206265 | B1 | 20031112 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| US 6498165 | B1 | 20021224 | US 2000-604305 | 2000 0626 |
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| JP 2003523942 | T | 20030812 | JP 2001-505922 | 2000 0626 |
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| AT 253915 | T | 20031115 | AT 2000-941701 | 2000 0626 |
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| PRIORITY APPLN. INFO.: | | | US 1999-141639P P | 1999 0630 |
| | | | <-- | |
| | | | WO 2000-US17443 W | 2000 0626 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 134:86271
ED Entered STN: 05 Jan 2001
AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-associated disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a

fused 6-membered aromatic ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl, or R3 and R5 taken together can represent :O; R3 or R5 can represent a 2 or 3 C methylene bridge forming a ring of 5-8 atoms fused to the A ring. R4 = H, Cl-C6-alkyl, C1-C6-alkoxyl. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted or unsubstituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5, X6 = independently N, C, optionally substituted CH. A ring = Ph, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, benzothienyl, benzofuranyl, indolyl, imidazolyl, benzimidazolyl, thiadiazolyl. R7, R8, R9, R10 = independently H, halo, OH, SH, CN, NO2, N3, N2+BF4-, alkyl, alkoxy, alkylthio, sulfinyl, sulfonyl, C1-C6-alkyl, C1-C6-perfluoroalkyl, acyl, alkoxycarbonyl, carbamoyl, acyloxy, alkoxycarbonyloxy, carbamoyloxy, amino, acylamino, ureido, sulfamoyl, sulfonylamino, two of R7, R8, R9, and R10 when on adjacent carbons join together to form a methylenedioxy bridge. N = 0-2. More than 500 example prepns. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:900457 HCAPLUS Full-text
DOCUMENT NUMBER: 134:56576
TITLE: Preparation of piperidinylmethylcyclopentanes as modulators of CCR-5 and/or CCR-3 chemokine receptors
INVENTOR(S): Finke, Paul E.; Hilfiker, Kerry A.; Loebach, Jennifer L.; Maccoss, Malcolm; Mills, Sander G.; Shen, Dong-ming; Oates, Bryan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 266 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076514 | A1 | 20001221 | WO 2000-US15769 | 20000608 |
| | | | <-- | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6432981 | B1 | 20020813 | US 2000-590484 | 20000608 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1999-138761P P | 19990611 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 134:56576
ED Entered STN: 22 Dec 2000
AB Title compds. I [X = alkylcycloalkylalkyl, alkenyl, alkynyl, alkyl-Y-alkyl, where Y = bond, O, SO2, NR10, NR10SO2, SO2NR10, S, and SO; R10 = H, (un)substituted alkyl,

benzyl, alkylcycloalkyl; R1 = CO2H, NO2, tetrazolyl, hydroxyisoxazole, etc; R2 = H, OH; R3 = (un)substituted Ph and heterocycle; Z = (CR4R5)n where n = 1-4; R4 and R5 = independently selected from H, OH, F, (un)substituted alkyl, cycloalkyl, alkenyl, alkynyl, Ph, etc., or R4 and R5 may be joined to form a 3-8 membered (un)substituted saturated ring; R7 = H, OH, halo, (un)substituted alkyl; R8 = H, (un)substituted cycloalkyl, Ph, naphthyl, biphenyl, and heterocycle; W = (CH2)x and A = (CH2)y where x or y is an integer from 0-2 with the provision the sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis, dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compd II·HCl was prepared in 5 steps from (+)-trans-3-formyl-4-phenylcyclopentan-1-one. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:900456 HCAPLUS Full-text
DOCUMENT NUMBER: 134:56575
TITLE: Preparation of piperidinylmethylcyclopentanes as modulators of CCR-5 and/or CCR-3 chemokine receptors
INVENTOR(S): Finke, Paul E.; Loebach, Jennifer L.; Maccoss, Malcolm; Mills, Sander G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076513 | A1 | 20001221 | WO 2000-US15765 | 2000 0608 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6506777 | B1 | 20030114 | US 2000-589972 | 2000 0608 |
| PRIORITY APPLN. INFO.: | | | US 1999-138872P P | 1999 0611 |

OTHER SOURCE(S): MARPAT 134:56575
ED Entered STN: 22 Dec 2000
AB Title compds. I [X = (un)substituted alkyl-Y-alkyl where Y = CO, CO2, OCO, OCONR9, NR9CO2, NR9CONR10; R9 = H, (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, alkenyl, alkynyl, benzyl or phenyl; R10 = H, (un)substituted alkyl, benzyl or phenyl; R9 and R10 may be joined together to form a 5-8 membered (un)substituted ring; R1 = CO2H, NO2, tetrazolyl, etc.; R2 = H, OH; R3 = (un)substituted Ph and heterocycle; Z = (CR4R5)n where n = 1-4; R4 and R5 = independently H, OH, F, (un)substituted alkyl, cycloalkyl, alkenyl, heterocycle, etc.; R4 and R5 may be joined together to form a 3-8 membered

(un)substituted saturated ring; R7 = H, OH, halo, (un)substituted alkyl; R8 = H, (un)substituted Ph, naphthyl, biphenyl, and heterocycle; W = (CH2)x and A = (CH2)y where x or y is an integer from 0-2 with the provision the sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis, dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compd II·HCl was prepared in 8 steps from Et trans-3-hydroxymethyl-4-phenylcyclopentylacetate. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:900455 HCAPLUS Full-text
DOCUMENT NUMBER: 134:56574
TITLE: Preparation of aminopiperidinylmethylcyclopentanes as modulators of CCR-5 and/or CCR-3 chemokine receptors
INVENTOR(S): Finke, Paul E.; Chapman, Kevin T.; Maccoss, Malcolm; Mills, Sander G.; Oates, Bryan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076512 | A1 | 20001221 | WO 2000-US15755 | 2000 0608 |

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| US 6500844 | B1 | 20021231 | US 2000-590487 | 2000 0608 |

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|---|---|---|
| PRIORITY APPLN. INFO.: | US 1999-139067P P | 1999 0611 |

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OTHER SOURCE(S): MARPAT 134:56574
ED Entered STN: 22 Dec 2000
AB Title compds. I [X = CONR9, NR9CO, OCONR9, NR9CO2, and NR9CONR10; R9 = H, alkyl, cycloalkyl, alkylcycloalkyl, benzyl, Ph, etc.; R10 = H, alkyl, benzyl, or (un)substituted phenyl; R9 and R10 may be joined together to form a 5-8 membered (un)substituted ring; Y = bond, CO, CO2, SO2NR9, alkyl, CONR9, C(S)NR9; Z = bond, NR9, O, alkyl; R1 = (un)substituted Ph, naphthyl, alkyl, cycloalkyl, heterocycle other than tetrazolyl, etc. with provision when Z = NR9, then R9 and R1 may be joined together to form a 5-8 membered (un)substituted cycloalkyl or heterocyclic ring; R2 = H, OH, or R2 and Z may be joined together to form a double bond; R3 = (un)substituted Ph or heterocycle; R7 = H, (un)substituted alkyl, OH, halo; R8 = alkyl, cycloalkyl, alkenyl, (un)substituted Ph, naphthyl, or heterocycle, etc.; W = (CH2)x and A = (CH2)y with

proviso that sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis, dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compound II was prepared in 7 steps from 4-oxo-2-phenylcyclopentanoic acid. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:900454 HCAPLUS Full-text
DOCUMENT NUMBER: 134:56573
TITLE: Preparation of piperidinylmethylcyclopentanes as modulators of CCR-5 and/or CCR-3 chemokine receptors
INVENTOR(S): Finke, Paul E.; Maccoss, Malcolm; Mills, Sander G.; Oates, Bryan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076511 | A1 | 20001221 | WO 2000-US15657 | 2000 0608 |
| | | | <-- | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6538002 | B1 | 20030325 | US 2000-591631 | 2000 0608 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1999-138763P | P 1999 0611 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 134:56573
ED Entered STN: 22 Dec 2000
AB Title compds. I [X = (un)substituted alkenyl, alkynyl, alkyl-Q-alkyl, wherein Q = bond, O, SO2, NR10, NR10SO2, SO2NR10, S, SO and R10 = H, alkyl, benzyl, Ph, etc; Y = bond, CO, CO2, OCO, SO2, alkyl, COR9, NR9CO, CSNR9, and NR9CS, wherein R9 = H, alkyl, cycloalkyl, benzyl, (un)substituted Ph, etc.; Z = bond, NR9, O, alkyl; R1 = (un)substituted Ph, naphthyl, heterocycle, alkyl, etc., or when Z = NR9, then R9 and R1 may be joined together to form a (un)substituted 5-8 membered alkyl or heterocyclic ring; R2 = H, OH, or R2 and % may be joined together to form a double bond; R3 = (un)substituted Ph or heterocycle; R7 = H, (un)substituted alkyl, OH, halo, Ph or R7 and R8 may be linked together through X to form a substituted 5-membered spirocycloalkyl or spiroheterocyclic derivative; R8 = H, cycloalkyl, Ph, naphthyl, biphenyl and (un)substituted heterocycle; W = (CH2)x and A = (CH2)y where x or y is an integer from 0-2 with the provision the sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis,

dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compound II was prepared in 7 steps from 4-oxo-2-phenylcyclopentanoic acid. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:725459 HCAPLUS Full-text
DOCUMENT NUMBER: 133:296373
TITLE: Preparation of 3-phenyl-4-(heterocyclylmethyl)pyrrolidine modulators of chemokine receptor activity
INVENTOR(S): Caldwell, Charles; Chapman, Kevin; Hale, Jeffrey; Kim, Dooseop; Lynch, Christopher; Maccoss, Malcolm; Mills, Sander G.; Willoughby, Christopher; Berk, Scott; Kim, Ronald M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000059498 | A1 | 20001012 | WO 2000-US9074 | 2000 0405 |
| | | | <-- | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6498161 | B1 | 20021224 | US 2000-543019 | 2000 0404 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1999-128172P | P 1999 0406 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 133:296373
ED Entered STN: 13 Oct 2000
AB The title compds. (I) [wherein R1 = CO2H, NO2, tetrazolyl, hydroxyisoxazole, SO2NH(alkyl)R9, or PO3H2; R9 = H, (cyclo)alkyl, benzyl, or (un)substituted phenyl; R2 = (un)substituted piperidinyl, tetrahydropyridinyl, piperazinyl, or 1-oxa-8-azaspiro[4.5]decyl; R3 = (un)substituted Ph or heterocyclyl; R4 = H or (un)substituted alkyl, (alkyl)cycloalkyl, alkenyl, alkynyl, Ph, alkylphenyl, naphthyl, biphenyl, heterocyclyl, cyclohexenyl, etc.; R5 and R6 = independently H or (un)substituted alkyl; or R4 and R5 may be joined together to form an (un)substituted C3-8 cycloalkyl ring; n = 1-3] were prepared as modulators of chemokine receptors, especially the chemokine receptors CCR-5 and/or CCR-3. For example, 2-(R)-((3-(R)-formyl)-4-(S)-3-fluorophenylpyrrolidinyl-1-yl)-3-cyclobutanepropionic acid benzyl ester (preparation given) was treated with Pd/C and dissolved in ClCH2CH2Cl. 4-[N-(pyrimid-2-yl)-N-(prop-

1- yl)amino]piperidine•HCl (4-step preparation given), NaBH(OAc)3, and TEA were added, followed by di-tert-butyldicarbonate, to give II. I showed binding activity to the CCR-5 or the CCR-3 receptor, generally with IC50 values of < 1 μM. The present invention is directed to compds. which inhibit the entry of human immunodeficiency virus (HIV) into target cells and are of value in the prevention and treatment of HIV infection and the resulting AIDS syndrome (no data). The invention is further directed to compds. which are useful in the prevention or treatment of certain inflammatory and immunoregulatory disorders, including asthma, allergic rhinitis, dermatitis, conjunctivitis, rheumatoid arthritis, and atherosclerosis (no data).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:725458 HCAPLUS Full-text
DOCUMENT NUMBER: 133:296372
TITLE: Preparation of 3-phenyl-4-(heterocyclylmethyl)pyrrolidine modulators of chemokine receptor activity
INVENTOR(S): Berk, Scott; Caldwell, Charles; Chapman, Kevin; Hale, Jeffrey; Lynch, Christopher; Maccoss, Malcolm; Mills, Sander G.; Willoughby, Christopher
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 200 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000059497 | A1 | 20001012 | WO 2000-US9059 | 2000 0405 |
| | | | <-- | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6399619 | B1 | 20020604 | US 2000-542898 | 2000 0404 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1999-128174P | P 1999 0406 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 133:296372
ED Entered STN: 13 Oct 2000
AB The title compds. (I) [wherein R1 = CO2H, NO2, tetrazolyl, hydroxyisoxazole, SO2NH(alkyl)R9, SO2NHCO(alkyl)R9, or PO3H2; R9 = H, (cyclo)alkyl, benzyl, or (un)substituted phenyl; R2 = (un)substituted piperidinyl, tetrahydropyridinyl, or piperazinyl; R3 = (un)substituted Ph or heterocyclyl; R4 = H or (un)substituted alkyl, (alkyl)cycloalkyl, alkenyl, alkynyl, Ph, alkylphenyl, naphthyl, biphenyl, heterocyclyl, cyclohexenyl, etc.; R5 and R6 = independently H or (un)substituted alkyl; or R4 and R5 may be joined together to form an (un)substituted C3-8 cycloalkyl ring; n = 1-3] were

prepared as modulators of chemokine receptors, especially the chemokine receptors CCR-5 and/or CCR-3. For example, EtNH2 and 1-tert-butoxycarbonyl-4-piperidone were reacted in the presence of DIEA and reduced with NaBH(OAc)3 to give 4-(N-ethylamino)-1-tert-butoxycarbonylpiperidine (97%). Addition of carbonyldiimidazole and 3,4-difluorobenzylamine to the piperidine followed by deprotection with TFA afforded 4-(N-(N-(3,4-difluorobenzyl)carbamoyl)-N- ethylamino)piperidine•TFA (45%). Coupling the deprotected piperidine with the aldehyde 2-(R)-(3-(R)-formyl-4-(S)- phenylpyrrolidin-1-yl)-2-(cyclohexyl)acetic acid 4-methoxybenzyl ester (preparation given) in the presence of DIEA followed by reduction with NaBH(OAc)3 gave II. I showed binding activity to the CCR-5 or the CCR-3 receptor, generally with IC50 values of < 1 μM. The present invention is directed to compds. which inhibit the entry of human immunodeficiency virus (HIV) into target cells and are of value in the prevention and treatment of HIV infection and the resulting AIDS syndrome (no data). The invention is further directed to compds. which are useful in the prevention or treatment of certain inflammatory and immunoregulatory disorders, including asthma, allergic rhinitis, dermatitis, conjunctivitis, rheumatoid arthritis, and atherosclerosis (no data).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:635463 HCAPLUS Full-text

DOCUMENT NUMBER: 131:243191

TITLE: Spiro-substituted azacycles as modulators of chemokine receptor activity

INVENTOR(S): Mills, Sander G.; MacCoss, Malcolm; Springer, Martin S.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: U.S., 97 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 5962462 | A | 19991005 | US 1997-989947 | | 1997 1212 |
| | | | <-- | | |
| PRIORITY APPLN. INFO.: | | | US 1996-32735P | P | 1996 1213 |
| | | | <-- | | |
| | | | US 1996-33558P | P | 1996 1220 |
| | | | <-- | | |

OTHER SOURCE(S): MARPAT 131:243191

ED Entered STN: 07 Oct 1999

AB The invention is directed to spiro-substituted azacycles which are useful as modulators of chemokine receptor activity. Specifically, I [R1 = H, (un)substituted alk(en/yn)yl; W = bond, (un)substituted alkylene; Q = (un)substituted NH, O, S, S(O), SO2; X = bond, (un)substituted alkylene, S, S(O), NHCO, OC(O), etc.; YZ = fused aryl or heteroaryl nucleus; m, n = 0 to 5; (m+n) = 1 to 5] were prepared The compds. are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4 (no data), and are thereby useful as antiinflammatory and immunomodulating agents. Use for the treatment of HIV infection and/or AIDS is claimed specifically. For instance, 1'-methylspiro[indoline-3,4'-piperidine] underwent a sequence of N-benzoyloxycarbonylation (71%), N'-demethylation (73%), reductive N'-alkylation with a corresponding polyfunctional aldehyde, and removal of the benzoyloxycarbonyl protecting group, to give title compound II.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

L132 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:574297 HCAPLUS Full-text
DOCUMENT NUMBER: 115:174297
TITLE: FK-506 and cyclosporin A: selective inhibition of calcium ionophore-induced polymorphonuclear leukocyte degranulation
AUTHOR(S): Forrest, Michael J.; Jewell, Marvin E.; Koo, Gloria C.; Sigal, Nolan H.
CORPORATE SOURCE: Dep. Immunol. Res., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Biochemical Pharmacology (1991), 42(6), 1221-8
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Nov 1991
AB This paper investigates the abilities of FK-506 and cyclosporin A (CsA) to inhibit human polymorphonuclear leukocyte (PMNL) degranulation. PMNLs, purified from human blood, were stimulated in vitro with A23187, ionomycin, the complement derived peptide C5a, formyl-methionylleucinylphenylalanine (FMLP) or phorbol myristate acetate (PMA). Degranulation was assessed by measuring the release of either lactoferrin or N-acetyl-β-D- glucosaminidase (NAG). Both FK-506 and CsA produced a concentration-related inhibition of degranulation induced by either A23187 or ionomycin but did not affect C5a-, FMLP- or PMA-induced degranulation. The IC50 values for inhibition of degranulation (approx. 0.7 nM for FK-506 and 33.7 nM for CsA) are very close to the published values for inhibition of human T-cell proliferation. Removal of calcium from the incubation medium with EGTA totally inhibited calcium ionophore-induced degranulation but had no effect against C5a-, FMLP- or PMA-induced degranulation. Preincubation of PMNLs with actinomycin D or cycloheximide did not affect either A23187- or PMA-induced degranulation. Non- immunosuppressive analogs of CsA were ineffective at inhibiting degranulation. Rapamycin, a macrolide structurally related to FK-506, did not inhibit degranulation but it did antagonize the inhibition produced by FK-506. Given the similar profiles of activity of FK-506 and CsA in neutrophils and T cells, the authors conclude that similar activation or signal transduction pathways may be present in both T cells and neutrophils. Because A23187-induced PMNL degranulation was not sensitive to either actinomycin D or cycloheximide, it is apparent that the signal transduction pathways ultimately control different cellular functions.

L132 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:61838 HCAPLUS Full-text
DOCUMENT NUMBER: 114:61838
TITLE: Process for synthesis of FK-506 C10-C18 intermediates
INVENTOR(S): Jones, Todd K.; Mills, Sander G.; Desmond, Richard
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4940797 | A | 19900710 | US 1989-327848 | 19890323 |
| | | | <-- | |
| EP 389244 | A1 | 19900926 | EP 1990-302981 | 1990 |

0320
<--
R: CH, DE, FR, GB, IT, LI, NL
CA 2012885 A1 19900923 CA 1990-2012885
1990
0322
<--
JP 03014529 A 19910123 JP 1990-72272
1990
0323
<--
PRIORITY APPLN. INFO.: US 1989-327848 A
1989
0323
<--
OTHER SOURCE(S): MARPAT 114:61838
ED Entered STN: 23 Feb 1991
AB The optically pure C10-C18 fragment of the immunosuppressant FK-506 was prepared by an improved process from I. (Me3CSiO)CH2CHMeCH2CH(OR)CH(BzO)CH(OR)CH2CHMeOCH2Ph (II; R = H) (preparation given) was converted to II where R = Me.

L132 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:164203 HCAPLUS Full-text
DOCUMENT NUMBER: 114:164203
TITLE: Preparation of substituted oxazolidinone as C8-18 fragment of FK-506
INVENTOR(S): Jones, Todd K.; Mills, Sander G.; Desmond, Richard
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 398474 | A2 | 19901122 | EP 1990-302982 | 1990 0320 |
| | | | <-- | |
| EP 398474 | A3 | 19910320 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| CA 2012884 | A1 | 19900922 | CA 1990-2012884 | 1990 0322 |
| | | | <-- | |
| JP 03135969 | A | 19910610 | JP 1990-72273 | 1990 0323 |
| | | | <-- | |
| JP 06062589 | B | 19940817 | | |
| US 5155228 | A | 19921013 | US 1991-702441 | 1991 0516 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1989-327849 A | 1989 0323 |
| | | | <-- | |
| | | | US 1990-559434 B1 | 1990 0725 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 114:164203
ED Entered STN: 03 May 1991
AB Title compds. I (P, P1 = hydroxy protectant; R1, R2 = H, (substituted C1-4 alkyl, -PhCH2, Ph, with proviso that R2 ≠ H) optically pure are prepared as intermediates for the immunosuppressant FK-506 or intermediates thereof. Title compound I (R1 = Ph; R2 = Me; P1 = 4-(MeO)C6H4CH2; P = PhCH2) was prepared from oxazolidone II.

L132 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:81436 HCAPLUS Full-text
DOCUMENT NUMBER: 114:81436
TITLE: Process for synthesis of FK-506 and tricarbonyl intermediates
INVENTOR(S): Jones, Todd K.; Askin, David; Mills, Sander G.; Reamer, Robert A.; Desmond, Richard; Volante, Ralph P.; Tschaen, David M.; Shinkai, Ichiro
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 378318 | A1 | 19900718 | EP 1990-300143 | 1990 0105 |
| | | | <-- | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| CA 2007490 | A1 | 19900711 | CA 1990-2007490 | 1990 0110 |
| | | | <-- | |
| JP 02233643 | A | 19900917 | JP 1990-4401 | 1990 0111 |
| | | | <-- | |
| US 5446158 | A | 19950829 | US 1990-596847 | 1990 1012 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1989-295877 A | 1989 0111 |
| | | | <-- | |
| | | | US 1989-375091 A | 1989 0630 |
| | | | <-- | |

OTHER SOURCE(S): MARPAT 114:81436
ED Entered STN: 09 Mar 1991
AB Claimed is a process for synthesizing tricarbonyl compds. RCOCOCOX (I) [R = (substituted) C1-40 alkyl; X = NR1R2, OR1, etc.; R1, R2 = C1-4 alkyl, benzyl, Ph, which may be substituted with halo, C1-4 alkoxy]. The said process comprises the steps of: a) contacting aldehyde RCHO with hydroxyl-protected acetate enolate equivalent Z1OCH:C(OM)X [Z1 = C1-10 alkyl, C6-10 aryl, benzyl (which can be substituted by halo or C1-4 alkoxy), trihydrocarbosilyl; M = Li, Na, K, etc.]; b) deprotecting the 2-hydroxyl function of the resulting product to form RCH(OH)CH(OH)COX (II); c) treating II in an inert, anhydrous, non-hydroxylic solvent with both oxalyl chloride and DMSO under an inert atmospheric at -78° to 0° followed by Et3N for a sufficient time to effect formation of I. Also claimed are intermediates for FK-506, e.g., piperidine III (R =

H, C1-10 alkyl; Z2 = H, trihydrocarbosilyl). The total synthesis of FK-506, a known immunosuppressant, is described.

L132 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:235036 HCAPLUS Full-text
DOCUMENT NUMBER: 112:235036
TITLE: Chemistry of tricarbonyl hemiketals and application of Evans technology to the total synthesis of the immunosuppressant (-)-FK-506
AUTHOR(S): Jones, Todd K.; Reamer, Robert A.; Desmond, Richard; Mills, Sander G.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065-0900, USA
SOURCE: Journal of the American Chemical Society (1990), 112(8), 2998-3017
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:235036
ED Entered STN: 23 Jun 1990
AB Details of model studies probing the chemical of the tricarbonyl region of FK-506 (I) are presented, and their use in designing a successful route to I is outlined. Applications of asym. oxazolidinone alkylation-aldol methodol. to a convergent, highly flexible synthesis of the C(10)-C(18) fragment and to improvements in the preparation of the C(20)-C(34) segment are also discussed.

L132 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:235199 HCAPLUS Full-text
DOCUMENT NUMBER: 112:235199
TITLE: Process for synthesis of hydroxylactone as intermediate for immunoregulant FK-506
INVENTOR(S): Mills, Sander G.; Volante, Ralph P.; Shinkai, Ichiro
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 343723 | A1 | 19891129 | EP 1989-201262 | 19890518 |
| | | | <-- | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| US 4940803 | A | 19900710 | US 1988-197551 | 19880523 |
| | | | <-- | |
| JP 02025475 | A | 19900126 | JP 1989-127978 | 19890523 |
| | | | <-- | |
| PRIORITY APPLN. INFO.: | | | US 1988-197551 A | 19880523 |
| | | | <-- | |

OTHER SOURCE(S): CASREACT 112:235199
ED Entered STN: 23 Jun 1990

AB Hydroxylactone I (R = H) (II) in optically pure form, useful as an intermediate in the synthesis of the C20-34 chain of the immunosuppressant FK-506 and useful as a precursor for producing an UV radiation absorber, is prepared To a suspension of quinic acid lactone I (R = OH) in ClCH2CH2Cl was added thiocarbonyldiimidazole at reflux under N to give 74% thioester III which was refluxed with Bu3SnH and AIBN in xylene under N to give 43% II.

L132 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:234809 HCAPLUS Full-text
DOCUMENT NUMBER: 112:234809
TITLE: Process for synthesis of E-2-methyl-α,β-unsaturated aldehydes as intermediates for the immunosuppressant FK-506 and as UV absorbers.
INVENTOR(S): Desmond, Richard; Mills, Sander G.; Volante, Ralph P.; Shinkai, Ichiro
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 343709 | A2 | 19891129 | EP 1989-201213 | 19890516 |
| | | | <-- | |
| EP 343709 | A3 | 19901205 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| US 4914220 | A | 19900403 | US 1989-316607 | 19890227 |
| | | | <-- | |
| JP 02025490 | A | 19900126 | JP 1989-127977 | 19890523 |
| | | | <-- | |
| JP 06000793 | B | 19940105 | | |
| PRIORITY APPLN. INFO.: | | | US 1988-197549 A | 19880523 |
| | | | <-- | |

OTHER SOURCE(S): CASREACT 112:234809; MARPAT 112:234809
ED Entered STN: 23 Jun 1990
AB The title compds. I (Z = triorganosilyl protecting group) are prepared from aldehydes II. I are also useful as UV absorbers (no data). Treatment of imine III with sec-BuLi, followed by reaction with aldehyde IV, treatment of the resulting product with CF3CO2H, and hydrolysis, gave 84% (E)-V.

L132 ANSWER 27 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:544668 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200544668
TITLE: Phosphate derivatives as immunoregulatory agents.
AUTHOR(S): Mandala, Suzanne [Inventor, Reprint author]; Bergstrom, James [Inventor]; Hajdu, Richard [Inventor]; Rosen, Hugh [Inventor]; Parsons, William [Inventor]; Card, Deborah J.

[Inventor]; Maccoss, Malcolm [Inventor]; Kathleen, Rupprecht [Inventor]
CORPORATE SOURCE: Scotch Plains, NJ, USA
ASSIGNEE: Merck and Co., Inc.
PATENT INFORMATION: US 6437165 20020820
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 20, 2002) Vol. 1261, No. 3. http://www.uspto.gov/web/menu/pat data.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
ED Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
AB Immunoregulatory compounds are disclosed of the formula: ##STR1## as well as the pharmaceutically acceptable salts and hydrates thereof, are disclosed. The compounds are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compositions and methods of use are included.

L132 ANSWER 28 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:505469 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200505469
TITLE: Substituted 3-amino biaryl propionic acids as potent VLA-4 antagonists.
AUTHOR(S): Kopka, Ihor E. [Reprint author]; Lin, Linus S.; Mumford, Richard A.; Lanza, Thomas, Jr.; Magriotis, Plato A.; Young, David; DeLaszlo, Stephen E.; MacCoss, Malcolm; Mills, Sander G.; Van Riper, Gail; McCauley, Ermengilda; Lyons, Kathryn; Vincent, Stella; Egger, Linda A.; Kidambi, Usha; Stearns, Ralph; Colletti, Adria; Teffera, Yohannes; Tong, Sharon; Owens, Karen; Levorse, Dorothy; Schmidt, John A.; Hagmann, William K.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, RY 123-136, PO Box 2000, Rahway, NJ, 07065, USA
ihor_kopka@merck.com
SOURCE: Bioorganic and Medicinal Chemistry Letters, (September, 2002) Vol. 12, No. 17, pp. 2415-2418. print.
CODEN: BMCLE8. ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
ED Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
AB A series of substituted N-(3,5-dichlorobenzenesulfonyl)-(L)-prolyl- and (L)-azetidyl-beta-biaryl beta-alanine derivatives was prepared as selective and potent VLA-4 antagonists. The 2,6-dioxygenated biaryl substitution pattern is important for optimizing potency. Oral bioavailability was variable and may be a result of binding to circulating plasma proteins.

L132 ANSWER 29 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:63645 BIOSIS Full-text
DOCUMENT NUMBER: PREV199598077945
TITLE: The Saccharomyces cerevisiae FKS1 (ETG1) gene encodes an integral membrane protein which is a subunit of 1,3-beta-D-glucan synthase.
AUTHOR(S): Douglas, Cameron M.; Foor, Forrest; Marrinan, Jean

A.; Morin, Nancy; Nielsen, Jennifer B.; Dahl, Arlene M.; Mazur, Paul; Baginsky, Walter; Li, Weili; El-Sherbeini, Mohamed; Clemas, Joseph A.; Mandala, Suzanne M.; Frommer, Beth R.; Kurtz, Myra B. [Reprint author]
CORPORATE SOURCE: Merck Res. Lab., PO Box 2000, Rahway, NJ 07065, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 26, pp. 12907-12911.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: Genbank-U12893
ENTRY DATE: Entered STN: 8 Feb 1995
Last Updated on STN: 14 Mar 1995
ED Entered STN: 8 Feb 1995
Last Updated on STN: 14 Mar 1995
AB In Saccharomyces cerevisiae, mutations in FKS1 confer hypersensitivity to the immunosuppressants FK506 and cyclosporin A, while mutations in ETG1 confer resistance to the cell-wall-active echinocandins (inhibitors of 1,3-beta-D-glucan synthase) and, in some cases, concomitant hypersensitivity to the chitin synthase inhibitor nikkomycin Z. The FKS1 and ETG1 genes were cloned by complementation of these phenotypes and were found to be identical. Disruption of the gene results in (i) a pronounced slow-growth phenotype, (ii) hypersensitivity to FK506 and cyclosporin A, (iii) a slight increase in sensitivity to echinocandin, and (iv) a significant reduction in 1,3-beta-D-glucan synthase activity in vitro. The nucleotide sequence encodes a 215-kDa polypeptide predicted to be an integral membrane protein with 16 transmembrane helices, consistent with previous observations that the etg1-1 mutation results in echinocandin-resistant glucan synthase activity associated with the nonextractable membrane fraction of the enzyme. These results suggest that FKS1 encodes a subunit of 1,3-beta-D-glucan synthase. The residual activity present in the disruption mutant, the nonessential nature of the gene, and results of Southern blot hybridization analysis point to the existence of a glucan synthase isozyme.

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=> d his l133

     (FILE 'HCAPLUS, MEDLINE, BIOSIS' ENTERED AT 12:49:36 ON 27 JUL
     2007)
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L8            36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
L9            67 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4N/RF
L10            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND L9
L11            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L11
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L14           36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L8
L15            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L10
L16           12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C3N/RF
L17            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L8
L18            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L11
L19           40 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND C6/RF AND
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                AND 1/P
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L34         10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
L35          5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND 20-30/C
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L38         32 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND 20-100/C
L41         68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND C6/RF
L42         68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 AND 12-50/C
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                L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19
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                L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35
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L44        199 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L41 OR L42 OR L43)
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L46            QUE  ABB=ON  PLU=ON  PHARMAC?/SC,SX
L47        483 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND L46
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L61          2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L60 AND L49
L68            QUE  ABB=ON  PLU=ON  AUTOIMMUN?
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L72            QUE  ABB=ON  PLU=ON  INFLAMMATION+PFT,OLD,NT/CT
L73         41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L72
L74            QUE  ABB=ON  PLU=ON  INFECTION+PFT,OLD,NT/CT
L75         15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L74
L76            QUE  ABB=ON  PLU=ON  AIDS+PFT,OLD,NT/CT
L77          7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L76
L78            QUE  ABB=ON  PLU=ON  ASTHMA+PFT,OLD,NT/CT
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L80            QUE  ABB=ON  PLU=ON  "RESPIRATORY SYSTEM, DISEASE"+PFT,
                OLD,NT/CT
L81         29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L80
L82            QUE  ABB=ON  PLU=ON  ARTHRITIS+PFT,OLD,NT/CT
L83         22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L82
L84            QUE  ABB=ON  PLU=ON  "MUSCULAR DYSTROPHY"+PFT,OLD,NT/CT
L85          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L84
L86            QUE  ABB=ON  PLU=ON  "SKIN, DISEASE"+PFT,OLD,NT/CT
L87         30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L86
L88            QUE  ABB=ON  PLU=ON  DERMATITIS+PFT,OLD,NT/CT
L89         12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L88
L90         68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 OR L61 OR L69 OR
                L71 AND L73 OR L75 OR L77 OR L79 OR L81 OR L83 OR L85
                OR L89 OR L87
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L95          44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L94
L96          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L90
L97        1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
                A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
                AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
                "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
                "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98             QUE  ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99          714 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L48
L100         228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99 AND L98
L101          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L50
L105         179 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 AND 18-70/C
L106          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L105
L133           4 SEA (L106 OR L96) AND L101


=> d l133 1-4 ibib ed abs fhitstr hitind

L133 ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:566538  HCAPLUS  Full-text
DOCUMENT NUMBER:          141:123484
TITLE:                    Preparation of 1-(amino)indanes and
                          (1,2-dihydro-3-amino)-benzofurans,
                          benzothiophenes and indoles as EDG receptor
                          agonists
INVENTOR(S):              Doherty, George A.; Hale,
                          Jeffrey J.; Mills, Sander G.
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 83 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2004058149        A2    20040715    WO 2003-US40129
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         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
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             KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,
             MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY,
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             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
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     AU 2003297232        A1    20040722    AU 2003-297232
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US 7220734 B2 20070522

PRIORITY APPLN. INFO.: US 2002-435381P P 2002 1220

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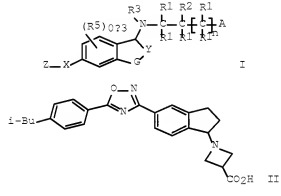
WO 2003-US40129 W 2003 1216


OTHER SOURCE(S): MARPAT 141:123484

ED Entered STN: 15 Jul 2004

GI



I



II


AB Compds. of formula I [G = C(R4)2, O, S, SO, SO2; X = Ph, alkyl, etc.; Y = (C(R4))p; Z = alkyl, heterocyclo, etc.; A = CO2H, PO3H2, SO3H, tetrazolyl, etc.; each R1 = H, halo, OH, alkyl, alkoxy; R2 = H, halo, OH, alkyl, alkoxy; R3 =H, alkyl; R2R3 = (substituted) alkylene; R4 = H, alkyl; R5 = halo, alkyl, alkoxy; n = 0-1; p = 1-3] are prepared as EDG receptor agonists. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, II was prepared from azetidine-3-carboxylic acid and the prepared indanone derivative The prepared compds. had > 100-fold selectivity of EDG1 over EDG3.


IT 350-92-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aminoindanes as immunosuppressants)

RN 350-92-5 HCAPLUS

CN 2-Propanone, 1,1,1-trifluoro-3-phenyl- (CA INDEX NAME)

IC ICM A61K
CC 25-23 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63
ST aminoindane prepn EDG receptor agonist; indane amino prepn EDG receptor agonist; immunosuppressant aminoindane prepn; benzofuran amino prepn EDG receptor agonist; benzothiophene amino prepn EDG receptor agonist; indole amino prepn EDG receptor agonist
IT Hepatitis
(B; preparation of aminoindanes as immunosuppressants)
IT Inflammation
(Crohn's disease; preparation of aminoindanes as immunosuppressants)
IT Intestine, disease
(Crohn's; preparation of aminoindanes as immunosuppressants)
IT Kidney, disease
(Goodpasture's syndrome; preparation of aminoindanes as immunosuppressants)
IT Eye, disease
Graves' disease
(Graves' ophthalmopathy; preparation of aminoindanes as immunosuppressants)
IT Nervous system, disease
(Guillain-Barre syndrome; preparation of aminoindanes as immunosuppressants)
IT Ear, disease
(Meniere's; preparation of aminoindanes as immunosuppressants)
IT Skin, neoplasm
(Sezary syndrome; preparation of aminoindanes as immunosuppressants)
IT Skin, neoplasm
(T-cell lymphoma; preparation of aminoindanes as immunosuppressants)
IT Disease, animal
(Vogt-Koyanagi-Harada's syndrome; preparation of aminoindanes as immunosuppressants)
IT Granulomatous disease
(Wegener's granulomatosis; preparation of aminoindanes as immunosuppressants)
IT Lung, disease
(acute injury; preparation of aminoindanes as immunosuppressants)
IT Injury
(acute pulmonary; preparation of aminoindanes as immunosuppressants)
IT Respiratory distress syndrome
(adult; preparation of aminoindanes as immunosuppressants)
IT Allergy
(allergic asthma; preparation of aminoindanes as immunosuppressants)
IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; preparation of aminoindanes as immunosuppressants)
IT Asthma
(allergic; preparation of aminoindanes as immunosuppressants)
IT Jaw
(alveolar bone; preparation of aminoindanes as immunosuppressants)

IT Edema
(angioneurotic; preparation of aminoindanes as immunosuppressants)
IT Erythropoiesis
(aplasia; preparation of aminoindanes as immunosuppressants)
IT Anemia (disease)
(aplastic; preparation of aminoindanes as immunosuppressants)
IT Alopecia
(areata; preparation of aminoindanes as immunosuppressants)
IT Dermatitis
(atopic; preparation of aminoindanes as immunosuppressants)
IT Anemia (disease)
Autoimmune disease
(autoimmune hemolytic anemia; preparation of aminoindanes as immunosuppressants)
IT Autoimmune disease
Inflammation
Thyroid gland, disease
(autoimmune thyroiditis; preparation of aminoindanes as immunosuppressants)
IT Hepatitis
(autoimmune; preparation of aminoindanes as immunosuppressants)
IT Infection
(bacterial; preparation of aminoindanes as immunosuppressants)
IT Cirrhosis
(biliary; preparation of aminoindanes as immunosuppressants)
IT Bronchi, disease
(bronchiectasis; preparation of aminoindanes as immunosuppressants)
IT Bronchi, disease
Inflammation
(bronchiolitis; preparation of aminoindanes as immunosuppressants)
IT Bronchi, disease
Inflammation
(bronchitis; preparation of aminoindanes as immunosuppressants)
IT Skin, disease
(bullous pemphigoid; preparation of aminoindanes as immunosuppressants)
IT Drug delivery systems
(capsules, soft; preparation of aminoindanes as immunosuppressants)
IT Drug delivery systems
(capsules; preparation of aminoindanes as immunosuppressants)
IT Lung, disease
(chronic obstructive pulmonary disease; preparation of aminoindanes as immunosuppressants)
IT Inflammation
(chronic; preparation of aminoindanes as immunosuppressants)
IT Dermatitis
(contact; preparation of aminoindanes as immunosuppressants)
IT Lymphoma
(cutaneous T-cell; preparation of aminoindanes as immunosuppressants)
IT Kidney, disease
(diabetic nephropathy; preparation of aminoindanes as

immunosuppressants)
IT Connective tissue, disease
Inflammation
(eosinophilic fasciitis; preparation of aminoindanes as immunosuppressants)
IT Granuloma
(eosinophilic; preparation of aminoindanes as immunosuppressants)
IT Skin, disease
(epidermolysis bullosa; preparation of aminoindanes as immunosuppressants)
IT Autoimmune disease
(exptl. autoimmune encephalomyelitis; preparation of aminoindanes as immunosuppressants)
IT Encephalomyelitis
(exptl. autoimmune; preparation of aminoindanes as immunosuppressants)
IT Kidney, disease
(failure; preparation of aminoindanes as immunosuppressants )
IT Lung, disease
(fibrosis; preparation of aminoindanes as immunosuppressants )
IT Ulcer
(gastric; preparation of aminoindanes as immunosuppressants )
IT Digestive tract, disease
Inflammation
(gastroenteritis; preparation of aminoindanes as immunosuppressants)
IT Gingiva, disease
Inflammation
(gingivitis; preparation of aminoindanes as immunosuppressants)
IT Inflammation
Kidney, disease
(glomerulonephritis; preparation of aminoindanes as immunosuppressants)
IT Transplant and Transplantation
(graft-vs.-host reaction; preparation of aminoindanes as immunosuppressants)
IT Kidney, disease
(hemolytic-uremic syndrome; preparation of aminoindanes as immunosuppressants)
IT Infection
(hepatitis B; preparation of aminoindanes as immunosuppressants)
IT Eye, disease
Infection
Inflammation
(herpetic keratitis; preparation of aminoindanes as immunosuppressants)
IT Skin, disease
(hyperproliferation; preparation of aminoindanes as immunosuppressants)
IT Skin, disease
(ichthyosis; preparation of aminoindanes as immunosuppressants)
IT Purpura (disease)
(idiopathic thrombocytopenic; preparation of aminoindanes as immunosuppressants)
IT Intestine, disease
(inflammatory; preparation of aminoindanes as immunosuppressants)
IT Drug delivery systems
(injections; preparation of aminoindanes as immunosuppressants)

IT Reperfusion
(injury; preparation of aminoindanes as immunosuppressants
)
IT Autoimmune disease
(insulin-dependent diabetes mellitus; preparation of aminoindanes as
immunosuppressants)
IT Diabetes mellitus
(insulin-dependent; preparation of aminoindanes as
immunosuppressants)
IT Inflammation
Kidney, disease
(interstitial nephritis; preparation of aminoindanes as
immunosuppressants)
IT Pneumonia
(interstitial; preparation of aminoindanes as
immunosuppressants)
IT Eye, disease
Inflammation
(keratitis; preparation of aminoindanes as
immunosuppressants)
IT Eye, disease
Inflammation
(keratoconjunctivitis; preparation of aminoindanes as
immunosuppressants)
IT Skin, disease
(leukoderma; preparation of aminoindanes as
immunosuppressants)
IT Skin, disease
(lichen planus; preparation of aminoindanes as
immunosuppressants)
IT Necrosis
(liver; preparation of aminoindanes as immunosuppressants)
IT Eye, disease
(macula, senile degeneration; preparation of aminoindanes as
immunosuppressants)
IT Alopecia
(male pattern; preparation of aminoindanes as
immunosuppressants)
IT Anemia (disease)
(megaloblastic anemia; preparation of aminoindanes as
immunosuppressants)
IT Carcinoma
(metastasis; preparation of aminoindanes as
immunosuppressants)
IT Headache
(migraine; preparation of aminoindanes as immunosuppressants
)
IT Erythema
(multiforme; preparation of aminoindanes as
immunosuppressants)
IT Liver, disease
(necrosis; preparation of aminoindanes as immunosuppressants
)
IT Inflammation
Nerve, disease
(neuritis; preparation of aminoindanes as immunosuppressants
)
IT Respiratory distress syndrome
(newborn; preparation of aminoindanes as immunosuppressants
)
IT Hepatitis
(non-A, non-B; preparation of aminoindanes as
immunosuppressants)
IT Diabetes mellitus
(non-insulin-dependent; preparation of aminoindanes as
immunosuppressants)
IT Respiratory system, disease

(obstructive; preparation of aminoindanes as immunosuppressants)
IT Inflammation
Pancreas, disease
(pancreatitis; preparation of aminoindanes as immunosuppressants)
IT Skin, disease
(pemphigus; preparation of aminoindanes as immunosuppressants)
IT Artery, disease
Inflammation
(periarteritis nodosa; preparation of aminoindanes as immunosuppressants)
IT Inflammation
Periodontium, disease
(periodontitis; preparation of aminoindanes as immunosuppressants)
IT Anemia (disease)
(pernicious anemia; preparation of aminoindanes as immunosuppressants)
IT Allergy
(photoallergic contact dermatitis; preparation of aminoindanes as immunosuppressants)
IT Dermatitis
(photoallergic contact; preparation of aminoindanes as immunosuppressants)
IT Myositis
(polymyositis; preparation of aminoindanes as immunosuppressants)
IT Immunosuppressants
(preparation of aminoindanes and amino-benzofurans, benzothiophenes and indoles as immunosuppressants)
IT AIDS (disease)
Acne
Addison's disease
Aging, animal
Agranulocytosis
Allergy
Alopecia
Arteriosclerosis
Asthma
Atherosclerosis
Autoimmune disease
Behcet's syndrome
Burn
Cataract
Celiac disease
Cirrhosis
Cough
Dermatitis
Dermatomyositis
Eczema
Emphysema
Eosinophilia
Erythema
Gingiva, disease
Graves' disease
Hyperthyroidism
Hypoxia
Immune disease
Lung, neoplasm
Lupus erythematosus
Lymph node, disease
Lymphocytic leukemia
Lymphoma
Mastocytoma
Multiple sclerosis

Muscular dystrophy
Myasthenia gravis
Myositis
Necrosis
Neoplasm
Obesity
Osteoporosis
Periodontium, disease
Pneumonia
Psoriasis
Respiratory system, disease
Rheumatic fever
Rheumatoid arthritis
Sarcoidosis
Seborrhea
Sepsis
Shock (circulatory collapse)
Sjogren syndrome
Thrombosis
Transformation, neoplastic
Transplant rejection
Ulcer
Urticaria
(preparation of aminoindanes as immunosuppressants)

IT Biliary tract, disease
(primary biliary cirrhosis; preparation of aminoindanes as immunosuppressants)

IT Inflammation
Intestine, disease
(pseudomembranous enterocolitis; preparation of aminoindanes as immunosuppressants)

IT Fibrosis
(pulmonary; preparation of aminoindanes as immunosuppressants)

IT Skin, disease
(pyoderma; preparation of aminoindanes as immunosuppressants)

IT Injury
(reperfusion; preparation of aminoindanes as immunosuppressants)

IT Eye, disease
Inflammation
(retinitis pigmentosa; preparation of aminoindanes as immunosuppressants)

IT Inflammation
Nose, disease
(rhinitis; preparation of aminoindanes as immunosuppressants)

IT Connective tissue, disease
(scleroderma; preparation of aminoindanes as immunosuppressants)

IT Biliary tract, disease
Inflammation
(sclerosing cholangitis; preparation of aminoindanes as immunosuppressants)

IT Mental and behavioral disorders
(senile psychosis; preparation of aminoindanes as immunosuppressants)

IT Shock (circulatory collapse)
(septic; preparation of aminoindanes as immunosuppressants)

IT Disease, animal
(siderosis; preparation of aminoindanes as immunosuppressants)

IT Drug delivery systems
(suspensions; preparation of aminoindanes as immunosuppressants)

IT lupus erythematosus
(systemic; preparation of aminoindanes as immunosuppressants
)
IT Drug delivery systems
(tablets; preparation of aminoindanes as immunosuppressants
)
IT Injury
(trauma; preparation of aminoindanes as immunosuppressants
)
IT Stomach, disease
(ulcer; preparation of aminoindanes as immunosuppressants)
IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of aminoindanes as
immunosuppressants)
IT Eye, disease
Inflammation
(uveitis; preparation of aminoindanes as immunosuppressants
)
IT Blood vessel, disease
Inflammation
(vasculitis; preparation of aminoindanes as
immunosuppressants)
IT Infection
(viral hepatitis; preparation of aminoindanes as
immunosuppressants)
IT Hepatitis
(viral; preparation of aminoindanes as immunosuppressants)
IT 721948-69-2P 721948-70-5P 721948-71-6P 721948-72-7P
721948-73-8P 721948-74-9P 721948-75-0P 721948-76-1P
721948-77-2P 721948-78-3P 721948-79-4P 721948-80-7P
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721948-85-2P 721948-86-3P 721948-87-4P 721948-88-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(preparation of aminoindanes as immunosuppressants)
IT 95-48-7, o-Cresol, reactions 350-92-5 623-51-8, Ethyl
mercaptoacetate 625-36-5, 3-Chloropropionyl chloride 629-27-6,
1-Iodooctane 2550-36-9, Bromomethylcyclohexane 3470-49-3,
5-Hydroxy-1-indanone 20029-52-1, 4-Cyclohexylbenzoic acid
25724-79-2, 5-Cyano-1-indanone 34598-49-7, 5-Bromo-1-indanone
36476-78-5, Azetidine-3-carboxylic acid 38861-88-0,
4-(2-Methylpropyl)benzoic acid 100202-39-9, Methyl
azetidine-3-carboxylate hydrochloride 146631-00-7,
4-Benzyloxyphenylboronic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoindanes as immunosuppressants)
IT 125114-88-7P 146936-34-7P 167279-18-7P
208108-76-3P 256488-46-7P 685529-03-7P
721948-89-6P 721948-90-9P 721948-91-0P 721948-92-1P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of aminoindanes as immunosuppressants)

L133 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:591193 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149520
TITLE: Preparation of aralkylpyrrolidines and
-azetidines as Edg receptor agonists
INVENTOR(S): Bugianesi, Robert L.; Doherty, George
A.; Gentry, Amy; Hale, Jeffrey J.
; Lynch, Christopher L.; Mills, Sander
G.; Neway, William E., III

PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003062252 | A1 | 20030731 | WO 2003-US1196 | 2003 0115 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
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| JP 2005515259 | T | 20050526 | JP 2003-562129 | 2003 0115 |
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| US 2005033055 | A1 | 20050210 | US 2004-500895 | 2004 0707 |
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| PRIORITY APPLN. INFO.: | | | US 2002-350000P P | 2002 0118 |
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OTHER SOURCE(S): MARPAT 139:149520
ED Entered STN: 01 Aug 2003
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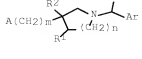


I

AB Title compds. I [Ar = (un)substituted Ph, naphthyl; A = CO2H, P(O)(OH)2, P(O)OH, SO3H, 1H-tetrazol-5-yl; R1, R2 = H, halogen, OH, CO2H, (un)substituted alkyl; R3 = H, (un)substituted alkyl; m, n = 0, 1] were prepared for use as Edg receptor agonists, useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 3-pyrrolidinol was converted to di-Et 3-hydroxypyrrolidin-3- ylphosphonate and treated with 4-nonylbenzaldehyde, followed by ester hydrolysis to give 1-(4-nonylbenzyl)-3-hydroxypyrrolidine-3- phosphonic acid.

IT 350-92-5, 1,1,1-Trifluoro-3-phenyl-2-propanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

RN 350-92-5 HCAPLUS

CN 2-Propanone, 1,1,1-trifluoro-3-phenyl- (CA INDEX NAME)

IC ICM C07F009-38

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST Edg receptor agonist aralkylpyrrolidine aralkylazetidine prepn immunosuppressant

IT Chronic lymphocytic leukemia
Human
Immunosuppressants
Lymphoma
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
Transplant rejection
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

IT Lupus erythematosus
(systemic; preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

IT 96-33-3, Methyl acrylate 100-83-4, 3-Hydroxybenzaldehyde 107-13-1, Acrylonitrile, reactions 111-70-6, 1-Heptanol 121-32-4, 3-Ethoxy-4-hydroxybenzaldehyde 121-33-5, 4-Hydroxy-3-methoxybenzaldehyde 123-08-0, 4-Hydroxybenzaldehyde 350-92-5, 1,1,1-Trifluoro-3-phenyl-2-propanone 406-94-0, trans-4,4,4-Trifluoro-2-butenoic acid 619-66-9, 4-Formylbenzoic acid 623-27-8, Terephthalaldehyde 623-51-8, Ethyl mercaptoacetate 629-27-6, 1-Iodooctane 682-30-4, Diethyl vinylphosphonate 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 2495-35-4, Benzyl acrylate 2973-76-4, 3-Bromo-4-hydroxy-5-methoxybenzaldehyde 2973-77-5, 3,5-Dibromo-4-hydroxybenzaldehyde 6138-90-5, Geranyl bromide 7770-45-8, 4-Hydroxy-1-naphthaldehyde 15174-69-3, 4-Hydroxy-3-methylbenzaldehyde 32247-96-4, 3,5-Bis(trifluoromethyl)benzyl bromide 36476-78-5, 3-Azetidinecarboxylic acid 38841-98-4, Octylmagnesium chloride 40499-83-0, 3-Hydroxypyrrolidine 54256-43-8, 4-Decylbenzoyl chloride 54963-70-1, 4-Nonylbenzoyl chloride 56962-11-9, 2-Chloro-4-hydroxybenzaldehyde 64283-87-0, 4-Phenylbutyl iodide 65695-05-8 93102-05-7 570424-02-1 570424-08-7 570424-09-8 570424-10-1 570424-11-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor

agonists)
IT 17012-21-4P 24076-33-3P, 3-Methoxy-4-(octyloxy)benzaldehyde 24083-12-3P, 3-Octyloxybenzaldehyde 24083-13-4P, 4-Octyloxybenzaldehyde 54784-14-4P, 4-(Octyloxy)-1-naphthaldehyde 59378-87-9P, 3-Pyrrolidinecarboxylic acid 62299-38-1P 70972-98-4P, 4-Nonylbenzaldehyde 70972-99-5P, 4-Decylbenzaldehyde 101385-93-7P 103057-44-9P 108898-23-3P 131888-48-7P 146976-34-7P 167279-18-7P 188846-99-2P 198959-37-4P 208108-76-3P 246847-91-6P 256488-46-7P 569684-92-0P 569684-93-1P 569684-95-3P 569685-33-2P 569685-34-3P 569685-42-3P 569685-43-4P 569685-49-0P 569685-50-3P 570423-86-8P 570423-87-9P 570423-88-0P 570423-89-1P 570423-90-4P 570423-91-5P 570423-92-6P 570423-93-7P 570423-94-8P 570423-95-9P 570423-96-0P 570423-97-1P 570423-98-2P 570423-99-3P 570424-00-9P 570424-01-0P 570424-03-2P 570424-04-3P 570424-05-4P 570424-06-5P 570424-07-6P 570424-13-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)
IT 570423-28-8P 570423-29-9P 570423-30-2P 570423-31-3P 570423-32-4P 570423-33-5P 570423-34-6P 570423-35-7P 570423-36-8P 570423-37-9P 570423-38-0P 570423-39-1P 570423-40-4P 570423-41-5P 570423-42-6P 570423-43-7P 570423-44-8P 570423-45-9P 570423-46-0P 570423-47-1P 570423-48-2P 570423-49-3P 570423-50-6P 570423-51-7P 570423-52-8P 570423-53-9P 570423-54-0P 570423-55-1P 570423-56-2P 570423-57-3P 570423-58-4P 570423-59-5P 570423-61-9P 570423-62-0P 570423-63-1P 570423-64-2P 570423-65-3P 570423-66-4P 570423-67-5P 570423-68-6P 570423-69-7P 570423-70-0P 570423-71-1P 570423-72-2P 570423-73-3P 570423-74-4P 570423-75-5P 570423-76-6P 570423-77-7P 570423-78-8P 570423-79-9P 570423-80-2P 570423-81-3P 570423-82-4P 570423-83-5P 570423-84-6P 570423-85-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)
IT 570424-12-3
RL: RCT (Reactant); RACT (Reactant or reagent)
('preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:591190 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149756
TITLE: Preparation of N-(benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists
INVENTOR(S): Doherty, George A.; Li, Chen; Hale, Jeffrey J.; Mills, Gander G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003062248 | A2 | 20030731 | Wo 2003-US1059 | 2003 0114 |
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| WO 2003062248 | A3 | 20060302 | | |
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| CA 2472713 | A1 | 20030731 | CA 2003-2472713 | 2003 0114 |
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| JP 2005527494 | T | 20050915 | JP 2003-562125 | 2003 0114 |
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| US 2005020837 | A1 | 20050127 | US 2004-500811 | 2004 0707 |
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| PRIORITY APPLN. INFO.: | | | US 2002-349995P P | 2002 0118 |
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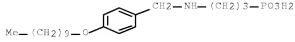
| | | | WO 2003-US1059 W | 2003 0114 |

OTHER SOURCE(S): MARPAT 139:149756
ED Entered STN: 01 Aug 2003
AB The present invention encompasses preparation of compds., A(CR1R2)nNHCHR3Ar{(R4)0-4}BC (Ar = Ph, naphthyl, etc.; A = CO2H, 1H-tetrazol-5-yl, PO3H2, PO2H2, SO3H, PO(R5)OH, R5 = C1-4 alkyl, hydroxyC1-4alkyl, Ph, COC1-3alkoxy, CH(OH)Ph, etc.; n = 2-4; R1, R2 = independently selected from H, halo, OH, CO2H, C1-6 alkyl, Ph, etc.; R3 = H, C1-4 alkyl, etc.; R4 = CO2H, C1-4 alkyl, sulfonylalkyl, alkoxy, alkoxycyclopropyl, aryl, aryloxy, etc.; C = C1-8 alkyl, C1-8 alkoxy, heterocyclyl, etc.; B = (un)substituted Ph, (un)substituted C5-16 alkyl, (un)substituted C5-16 alkenyl, (un)substituted C5-16 alkynyl, etc.), as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, reaction of 3-aminopropylphosphonic acid with 4-(decyloxy)benzaldehyde in presence of Bu4NOH and sodium cyanoborohydride in MeOH for 1h at 50° gave title compound, N-((4-decyloxy)benzyl)-3-aminopropylphosphonic acid.
IT 569682-66-2P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

RN 569682-66-2 HCAPLUS

CN Phosphonic acid, [3-[[[4-(decyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)




IC ICM C07F

CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1, 63

IT Inflammation
(Crohn's disease; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Asthma
(Graves ophthalmopathy; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Lymphoma
(acute and chronic; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Arthritis
(chronic rheumatoid; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Inflammation
(chronic; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Skin, disease
(ichthyosis, bullous; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Autoimmune disease
(insulin-dependent diabetes mellitus; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Autoimmune disease
Cardiovascular agents
Cardiovascular system
Chronic lymphocytic leukemia
Cirrhosis
Drug delivery systems
Human
Immunosuppressants
Immunosuppression
Mammalia
Multiple sclerosis
(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Lupus erythematosus
(systemic; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Inflammation

Intestine, disease
(ulcerative colitis; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Eye, disease
Inflammation
(uveitis; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT 569682-66-2P 569682-67-3P 569682-68-4P
569682-69-5P 569682-70-8P 569682-71-9P
569682-72-0P 569682-73-1P 569682-74-2P
**569682-75-3P** 569682-76-4P 569682-77-5P
569682-78-6P 569682-79-7P 569682-80-0P 569682-81-1P
**569682-82-2P** 569682-83-3P 569682-84-4P 569682-85-5P
**569682-86-6P** 569682-87-7P 569682-88-8P
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**569684-61-3P** 569684-62-4P 569684-63-5P
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**569684-70-4P** 569684-71-5P 569684-72-6P 569684-73-7P
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569684-87-3P 569684-88-4P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT 56-12-2, reactions 64-04-0, Benzeneethanamine 75-07-0, Acetaldehyde, reactions 83-38-5 98-80-6, Phenylboronic acid 100-52-7, Benzaldehyde, reactions 103-63-9, Phenethyl bromide 106-41-2, 4-Bromophenol 107-08-4, 1-Iodopropane 107-13-1, Acrylonitrile, reactions 107-95-9, β-Alanine 111-70-6, 1-Heptanol 111-86-4, Octylamine 112-31-2, n-Decanal

121-32-4, 3-Ethoxy-4-hydroxybenzaldehyde 121-33-5 123-08-0, 4-Hydroxybenzaldehyde 123-38-6, Propanal, reactions 139-85-5, 3,4-Dihydroxybenzaldehyde 143-16-8 144-90-1 350-92-5 437-81-0 541-48-0 542-69-8, 1-Iodobutane 556-18-3, 4-Aminobenzaldehyde 565-71-9 589-29-7, 1,4-Benzenedimethanol 591-20-8, 3-Bromophenol 616-76-2 619-66-9, 4-Carboxybenzaldehyde 623-27-8, 1,4-Benzenedicarboxaldehyde 623-51-8, Ethyl mercaptoacetate 629-27-6, 1-Iodooctane 637-59-2 638-45-9, 1-Iodohexane 660-88-8 764-85-2, Nonanoyl chloride 924-49-2 2050-77-3, 1-Iododecane 2052-07-5 2113-57-7 2233-18-3 2314-36-5 2374-05-2, 4-Bromo-2,6-dimethylphenol 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 2439-54-5 2973-76-4 2973-78-6 3111-37-3 3132-99-8, 3-Bromobenzaldehyde 3261-62-9 7300-51-4 3453-33-6, 6-Methoxy-2-naphthaldehyde 3761-92-0, Hexylmagnesium bromide 3964-56-5 4282-40-0, 1-Iodoheptane 4282-42-2, 1-Iodononane 4282-44-4, 1-Iodoundecane 4815-96-7 5438-36-8 5699-54-7 6323-99-5 7013-05-0 7368-78-7, 4-Bromo-2-methoxyphenol 7463-51-6, 4-Bromo-3,5-dimethylphenol 7530-27-0 7770-45-8 10521-91-2, 5-Phenyl-1-pentanol 13138-33-5, 3-Aminopropylphosphonic acid 13214-66-9, Benzenebutanamine 13477-53-7 13880-74-5 18278-34-7, 4-Hydroxy-2-methoxybenzaldehyde 19463-48-0 23703-22-2 25006-17-1 35622-27-6 38841-98-4, Octylmagnesium chloride 40371-51-5 49763-66-8, 4-Octylbenzaldehyde 51554-95-1 56217-93-7, 1H-Tetrazole-5-propanamine 56962-11-9, 2-Chloro-4-hydroxybenzaldehyde 58521-63-4 64283-87-0 65564-05-8, 3-(Benzyloxycarbonylamino)propanal 65600-74-0, Ethyldiethoxymethyl phosphinate 65695-05-8 70547-87-4 70972-98-4, 4-Nonylbenzaldehyde 70972-99-5 76287-49-5 76542-24-0, 1-Bromo-4-(nonylthio)benzene 103680-71-3 127729-35-5 130592-02-8 148547-19-7, Methyl 4-bromo-3-methylbenzoate 495397-19-8 569684-89-5 569685-44-5 569685-48-9 569685-53-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT 24076-33-3P 24083-13-4P, 4-Octyloxybenzaldehyde 30609-20-2P 50262-46-9P 54784-14-4P 56308-79-3P 56741-21-0P 60951-75-9P 61343-82-6P 71434-34-9P 75472-36-5P 75677-08-6P 78119-82-1P, 6-Hydroxy-2-naphthaldehyde 83697-65-8P 93972-07-7P 93972-08-8P 99186-35-3P, 4-Hydroxy-3-propyloxybenzaldehyde 101500-22-5P 103680-62-2P 108898-23-3P 121118-78-3P 123912-25-4P 131888-48-7P 143230-66-4P 149104-89-2P, 4-Bromo-3-methylbenzyl alcohol 167279-18-7P 169806-13-7P 208108-76-3P 221018-00-4P, [1,1':2',1''-Terphenyl]-4-carboxaldehyde 226408-14-6P, [1,1':3',1''-Terphenyl]-4-carboxaldehyde 246847-91-6P 256488-46-7P 500191-05-9P 569684-90-8P 569684-91-9P 569684-92-0P 569684-93-1P 569684-94-2P 569684-95-3P 569684-96-4P 569684-97-5P 569684-98-6P 569684-99-7P 569685-00-3P 569685-01-4P 569685-02-5P 569685-03-6P 569685-04-7P 569685-05-8P 569685-06-9P 569685-07-0P 569685-08-1P 569685-09-2P 569685-10-5P 569685-11-6P 569685-12-7P 569685-13-8P 569685-14-9P 569685-15-0P 569685-16-1P 569685-17-2P 569685-18-3P 569685-19-4P 569685-20-7P 569685-21-8P 569685-22-9P 569685-23-0P 569685-24-1P 569685-25-2P 569685-26-3P 569685-27-4P 569685-28-5P 569685-29-6P 569685-30-9P 569685-31-0P 569685-32-1P 569685-33-2P 569685-34-3P 569685-35-4P 569685-36-5P 569685-37-6P 569685-38-7P 569685-39-8P 569685-40-1P 569685-41-2P 569685-42-3P 569685-43-4P 569685-45-6P 569685-46-7P 569685-47-8P 569685-49-0P 569685-50-3P 569685-51-4P 569685-52-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)
(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

L133 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:590932 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149413
TITLE: Selective S1P1/Edg1 receptor agonists
INVENTOR(S): Doherty, George A.; Forrest, Michael J.; Hajdu, Richard; Hale, Jeffrey J.; Li, Chen; Mandala, Suzanne M.; Mills, Sander G.; Rosen, Hugh; Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003061567 | A2 | 20030731 | WO 2003-US1120 | 2003 0114 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
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| US 2005070506 | A1 | 20050331 | US 2004-501176 | 2004 0712 |
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| PRIORITY APPLN. INFO.: | | | US 2002-349991P | P |

2002
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WO 2003-US1120 W
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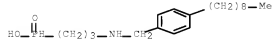
ED Entered STN: 01 Aug 2003
AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.
IT 569684-52-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
RN 569684-52-2 HCAPLUS
CN Phosphinic acid, [3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)




IC ICM A61K
CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1, 10, 25, 63
IT Hepatitis
(B, acute; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
(Crohn's disease; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Intestine, disease
(Crohn's; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-1 (endothelial differentiation gene 1); preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(EDG-3 (endothelial differentiation gene 3); preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Anemia (disease)
(Fanconi's; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Kidney, disease
(Goodpasture's syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Eye, disease
Graves' disease
(Graves' ophthalmopathy; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Nervous system, disease
(Guillain-Barre syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Ear, disease
(Meniere's; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Skin, neoplasm
(Sezary syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Skin, neoplasm
(T-cell lymphoma; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Disease, animal
(Vogt-Koyanagi-Harada's syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Granulomatous disease
(Wegener's granulomatosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Infection
(acute hepatitis B; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Edema
(angioneurotic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Erythropoiesis
(aplasia; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Anemia (disease)
(aplastic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Alopecia

(areata; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Dermatitis
(atopic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Chemotherapy
(augmentation of; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Anemia (disease)
Autoimmune disease
(autoimmune hemolytic anemia; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Autoimmune disease
Inflammation
Thyroid gland, disease
(autoimmune thyroiditis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Hepatitis
(autoimmune; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Infection
(bacterial; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Cirrhosis
(biliary; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Bronchi, disease
Inflammation
(bronchitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Skin, disease
(bullous pemphigoid; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
(carditis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Dermatitis
(contact; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Lymphoma
(cutaneous T-cell; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Connective tissue, disease
Inflammation
(eosinophilic fasciitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Skin, disease
(epidermolysis bullosa; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Autoimmune disease
(exptl. autoimmune encephalomyelitis; preparation of amino functionalized organo phosphonates or organo carboxylates as

S1P1/Edg1 receptor agonists)
IT Encephalomyelitis
(exptl. autoimmune; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Kidney, disease
(failure, acute, ischemic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Kidney, disease
(failure, chronic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Liver, disease
(failure; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Digestive tract, disease
Inflammation
(gastroenteritis, eosinophilic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Gingiva, disease
Inflammation
(gingivitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
Kidney, disease
(glomerulonephritis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Hair preparations
(growth stimulants; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Kidney, disease
(hemolytic-uremic syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Eye, disease
Infection
Inflammation
(herpetic keratitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Skin, disease
(hyperproliferation; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Skin, disease
(ichthyosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Purpura (disease)
(idiopathic thrombocytopenic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Intestine, disease
(inflammatory; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
Kidney, disease
(interstitial nephritis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Pneumonia
(interstitial; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Eye, disease
Inflammation
(keratitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Eye, disease
Inflammation
(keratoconjunctivitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Skin, disease
(lichen planus; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Necrosis
(liver, acute; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Eye, disease
(macula, senile degeneration; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Anemia (disease)
(megaloblastic anemia; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Carcinoma
(metastasis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Headache
(migraine; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Erythema
(multiforme; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Heart, disease
Inflammation
(myocarditis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Liver, disease
(necrosis, acute; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
Nerve, disease
(neuritis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Hepatitis
(non-A, non-B; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
Pancreas, disease
(pancreatitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Skin, disease
(pemphigus foliaceus; preparation of amino functionalized organo

phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Artery, disease
Inflammation
(periarteritis nodosa; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Inflammation
Periodontium, disease
(periodontitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Anemia (disease)
(pernicious anemia; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Allergy
(photoallergic contact dermatitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Dermatitis
(photoallergic contact; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Allergy
(pollen; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Myositis
(polymyositis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT AIDS (disease)
Acne
Addison's disease
Aging, animal
Agranulocytosis
Allergy inhibitors
Anti-AIDS agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarteriosclerotics
Antiarthritics
Antiasthmatics
Antibacterial agents
Anticoagulants
Antidiabetic agents
Antihistamines
Antimigraine agents
Antitumor agents
Antiulcer agents
Arteriosclerosis
Asthma
Atherosclerosis
Behcet's syndrome
Blood coagulation
Celiac disease
Chronic lymphocytic leukemia
Cirrhosis
Dermatomyositis
Diabetes mellitus
Drug screening
Eczema
Emphysema
Eosinophilia
Erythema
Gingiva, disease

Graves' disease
Human
Hyperthyroidism
Hypoxia
Immunosuppressants
Ischemia
Leukotriene antagonists
Lung, neoplasm
Lymphocytic leukemia
Lymphoma
Mastocytoma
Multiple sclerosis
Muscular dystrophy
Myasthenia gravis
Myositis
Nervous system agents
Osteoporosis
Periodontium
Psoriasis
Rheumatic fever
Rheumatoid arthritis
Sarcoidosis
Sepsis
Sjogren syndrome
Transformation, neoplastic
Transplant rejection
Urticaria
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Inflammation
Intestine, disease
(pseudomembranous enterocolitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Skin, disease
(pyoderma; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Inflammation
(rectal; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Intestine, disease
(rectum, inflammation; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Eye, disease
Inflammation
(retinitis pigmentosa; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Inflammation
Nose, disease
(rhinitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Connective tissue, disease
(scleroderma; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Biliary tract, disease
Inflammation
(sclerosing cholangitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Mental and behavioral disorders

(senile psychosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Shock (circulatory collapse)
(septic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Disease, animal
(siderosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Lupus erythematosus
(systemic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Injury
(trauma; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Shock (circulatory collapse)
(traumatic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Respiratory system, disease
(treatment; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Eye, disease
Inflammation
(uveitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Blood vessel, disease
Inflammation
(vasculitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Infection
(viral hepatitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT Hepatitis
(viral; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT 569684-52-2P 569684-61-3P 571206-20-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
IT 569682-66-2P 569682-67-3P 569682-68-4P
569682-69-5P 569682-70-8P 569682-71-9P
569682-72-0P 569682-73-1P 569682-74-2P
569682-75-3P 569682-77-5P 569682-78-6P
569682-79-7P 569682-80-0P 569682-81-1P 569682-82-2P
569682-83-3P 569682-84-4P 569682-85-5P 569682-86-6P
569682-87-7P 569682-89-9P 569682-91-3P
569682-93-5P 569682-95-7P 569682-97-9P
569683-99-1P 569683-01-8P 569683-03-0P
569683-05-2P 569683-07-4P 569683-09-6P 569683-11-0P

569683-13-2P 569683-15-4P 569683-17-6P 569683-21-2P
569683-23-4P 569683-25-6P 569683-27-8P 569683-28-9P
569683-30-3P 569683-32-5P 569683-34-7P
569683-39-2P 569683-41-6P 569683-43-8P
569683-45-0P 569683-47-2P 569683-49-4P
569683-51-8P 569683-55-2P 569683-57-4P
569683-59-6P 569683-61-0P 569683-63-2P
569683-67-6P 569683-68-7P 569683-70-1P
569683-72-3P 569683-74-5P 569683-76-7P
569683-78-9P 569683-81-4P 569683-82-5P
569683-87-0P 569683-89-2P 569683-90-5P
569683-92-7P 569683-94-9P 569683-96-1P
569683-99-4P 569684-01-1P 569684-03-3P
569684-05-5P 569684-07-7P 569684-09-9P
569684-11-7P 569684-13-9P 569684-15-1P
569684-17-3P 569684-19-5P 569684-21-9P
569684-23-1P 569684-25-3P 569684-26-0P
569684-27-1P 569684-28-2P 569684-30-6P
569684-32-8P 569684-34-0P 569684-39-5P
569684-41-9P 569684-46-4P 569684-47-5P
569684-48-6P 569684-49-7P 569684-50-0P
569684-51-1P 569684-53-3P 569684-54-4P
569684-55-5P 569684-57-7P 569684-58-8P
569684-59-9P 569684-62-4P 569684-64-6P
569684-65-7P 569684-66-8P 569684-67-9P
569684-68-0P 569684-69-1P 569684-70-4P 569684-71-5P
569684-72-6P 569684-73-7P 569684-74-8P
569684-76-0P 569684-77-1P 569684-78-2P
569684-79-3P 569684-80-6P 569684-81-7P
569684-82-8P 569684-83-9P 569684-84-0P
569684-85-1P 569684-86-2P 569684-87-3P
569684-88-4P 570423-28-8P 570423-29-9P
570423-30-2P 570423-31-3P 570423-32-4P
570423-33-5P 570423-34-6P 570423-35-7P
570423-38-0P 570423-39-1P 570423-40-4P
570423-41-5P 570423-42-6P 570423-43-7P
570423-45-9P 570423-46-0P 570423-47-1P
570423-48-2P 570423-49-3P 570423-50-6P
570423-51-7P 570423-52-8P 570423-53-9P
570423-54-0P 570423-55-1P 570423-56-2P
570423-57-3P 570423-58-4P 570423-59-5P 570423-61-9P
570423-62-0P 570423-63-1P 570423-64-2P
570423-65-3P 570423-66-4P 570423-67-5P
570423-68-6P 570423-73-3P 570423-74-4P
570423-75-5P 570423-76-6P 570423-77-7P
570423-78-8P 570423-79-9P 570423-80-2P
570423-81-3P 571206-07-0P 571206-08-1P
571206-09-2P 571206-10-5P 571206-11-6P
571206-12-7P 571206-13-8P 571206-14-9P 571206-15-0P
571206-16-1P 571206-17-2P 571206-18-3P
571206-19-4P 571206-21-8P 571206-27-4P
571206-28-5P 571206-29-6P 571206-36-5P
571206-37-6P 571206-38-7P 571206-40-1P
571206-41-2P 571206-42-3P 571206-43-4P
571206-44-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT 56-12-2, 4-Aminobutanoic acid, reactions 64-04-0, Phenethylamine 96-33-3, Methyl acrylate 98-80-6, Phenylboronic acid 100-83-4, 3-Hydroxybenzaldehyde 106-41-2, 4-Bromophenol 107-13-1, Acrylonitrile, reactions 111-70-6, 1-Heptanol 111-86-4, 1-Octanamine 121-32-4, 3-Ethoxy-4-hydroxybenzaldehyde 121-33-5, 4-Hydroxy-3-methoxybenzaldehyde 123-08-0,

4-Hydroxybenzaldehyde 139-85-5, 3,4-Dihydroxybenzaldehyde 143-16-8, Dihexylamine 850-42-5, 1,1,1-Trifluoro-3-phenyl-2-propanone 401-95-6, 3,5-Bis(trifluoromethyl)benzaldehyde 542-69-8, 1-Iodobutane 556-18-3, 4-Aminobenzaldehyde 589-29-7, 1,4-Benzenedimethanol 591-20-8, 3-Bromophenol 619-66-9, 4-Formylbenzoic acid 623-27-8, Terephthalaldehyde 629-27-6, 1-Iodooctane 637-59-2, 1-Bromo-3-phenylpropane 638-45-9, 1-Iodohexane 682-30-4, Diethyl vinylphosphonate 924-49-2, 4-Amino-3-hydroxybutanoic acid 2052-07-5, 2-Bromobiphenyl 2113-57-7, 3-Bromobiphenyl 2233-18-3, 4-Hydroxy-3,5-dimethylbenzaldehyde 2314-36-5, 3,5-Dichloro-4-hydroxybenzaldehyde 2374-05-2, 4-Bromo-2,6-dimethylphenol 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 2439-54-5, N-Methyloctylamine 2495-35-4, Benzyl acrylate 2973-76-4, 3-Bromo-4-hydroxy-5-methoxybenzaldehyde 2973-77-5, 3,5-Dibromo-4-hydroxybenzaldehyde 2973-78-6, 3-Bromo-4-hydroxybenzaldehyde 3111-37-3, 3-Bromo-5-ethoxy-4-hydroxybenzaldehyde 3132-99-8, 3-Bromobenzaldehyde 3261-62-9, 4-Methylphenethylamine 3300-51-4, 4-Trifluoromethylbenzylamine 3453-33-6, 6-Methoxy-2-naphthaldehyde 3761-92-0, Hexylmagnesium bromide 3964-56-5, 4-Bromo-2-chlorophenol 4282-40-0, 1-Iodoheptane 4282-42-2, 1-Iodononane 4282-44-4, 1-Iodoundecane 4815-96-7, 3-Bromo-5-benzyloxy-4-hydroxybenzaldehyde 5438-36-8, 4-Hydroxy-3-iodo-5-methoxybenzaldehyde 6138-90-5, Geranyl bromide 6323-99-5 7368-78-7, 4-Bromo-2-methoxyphenol 7463-51-6, 4-Bromo-3,5-dimethylphenol 7530-27-0, 4-Bromo-2-chloro-6-methylphenol 7770-45-8, 4-Hydroxy-1-naphthaldehyde 10521-91-2, 5-Phenyl-1-pentanol 13138-33-5, 3-Aminopropylphosphonic acid 13214-66-9, Benzenebutanamine 13477-53-7, 4-Amino-2-hydroxybutanoic acid 13631-21-5, 4-Bromo-3-chlorophenol 13880-74-5, 4-Aminopentanoic acid 15174-69-3, 4-Hydroxy-3-methylbenzaldehyde 18278-34-7, 4-Hydroxy-2-methoxybenzaldehyde 19463-48-0, 3-Chloro-4-hydroxy-5-methoxybenzaldehyde 23703-22-2, 1-Bromo-4-hexylbenzene 25006-17-1, 4-Hydroxy-3-methoxy-5-propylbenzaldehyde 35622-27-6, 4-Aminobutylphosphonic acid 36476-78-5, 3-Azetidinecarboxylic acid 38841-98-4, Octylmagnesium chloride 40499-83-0, 3-Pyrrolidinol 50773-56-3, 3-Benzyloxy-4-hydroxybenzaldehyde 51572-88-4, 4-Formyl-2-hydroxybenzoic acid 54256-43-8, 4-Decylbenzoyl chloride 54963-70-1, 4-Nonylbenzoyl chloride 56217-93-7, 5-(3-Aminopropyl)-1H-tetrazole 56962-11-9, 2-Chloro-4-hydroxybenzaldehyde 64283-87-0, 4-Iodobutylbenzene 65564-05-8, 3-Benzyloxycarbonylaminopropanal 65600-74-0, Ethyl diethoxymethylphosphinate 70547-87-4, 4-Hydroxy-2,6-dimethylbenzaldehyde 76542-24-0, 1-Bromo-4-nonylthiobenzene 87199-17-5, 4-Formylphenylboronic acid 93102-05-7 103680-71-3 130592-02-8, 4-Amino-2,2-difluorobutanoic acid 148547-19-7, Methyl 4-bromo-3-methylbenzoate 569684-89-5, 4-Amino-3-fluorobutanoic acid 569685-48-9 570424-08-7 570424-09-8 570424-10-1 570424-11-2 570424-12-3 571206-46-7, 4-Hydroxy-3-methoxy-5-propylthiobenzaldehyde 571206-48-9, 4-Nonylbenzyl iodide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT 1203-68-5P, [1,1'-Biphenyl]-2-carboxaldehyde 1204-60-0P, [1,1'-Biphenyl]-3-carboxaldehyde 6853-57-2P 17012-21-4P 24076-33-3P 24083-12-3P, 3-Octyloxybenzaldehyde 24083-13-4P, 4-Octyloxybenzaldehyde 49763-67-9P 49763-69-1P 50262-46-9P 54784-14-4P 56308-79-3P 59378-87-9P, 3-Pyrrolidinecarboxylic acid 60951-75-9P 61343-82-6P 62299-38-1P 70972-98-4P, 4-Nonylbenzaldehyde 70972-99-5P, 4-Decylbenzaldehyde 75472-36-5P 75677-08-6P 80407-63-2P 83697-65-8P 101385-93-7P 101500-22-5P 103057-44-9P 103680-62-2P

108898-23-3P 110943-74-3P 121118-78-3P 131888-48-7P
146936-34-7P 149104-89-2P 167279-18-7P
169806-13-7P 188546-93-3P 198959-37-4P
208198-75-3P 246847-91-6P 256438-46-7P
500191-05-9P 569684-90-8P 569684-91-9P 569684-92-0P
569684-93-1P 569684-94-2P 569684-95-3P 569684-96-4P
569684-97-5P 569684-98-6P 569684-99-7P 569685-00-3P
569685-01-4P 569685-02-5P 569685-03-6P 569685-04-7P
569685-07-0P 569685-08-1P 569685-09-2P 569685-10-5P
569685-12-7P 569685-13-8P 569685-14-9P
569685-15-0P 569685-16-1P 569685-17-2P
569685-18-3P 569685-19-4P 569685-20-7P
569685-21-8P 569685-22-9P 569685-24-1P
569685-25-2P 569685-26-3P 569685-27-4P
569685-29-6P 569685-30-9P 569685-31-0P 569685-32-1P
569685-33-2P 569685-34-3P 569685-35-4P 569685-36-5P
569685-37-6P 569685-38-7P 569685-39-8P
569685-40-1P 569685-41-2P 569685-42-3P
569685-43-4P 569685-45-6P 569685-46-7P
569685-49-0P 569685-50-3P 569685-51-4P
569685-52-5P 570423-86-8P 570423-87-9P 570423-89-1P
570423-91-5P 570423-92-6P 570423-93-7P
570423-94-8P 570423-95-9P 570423-96-0P
570423-97-1P 570423-98-2P 570423-99-3P
570424-00-9P 570424-01-0P 570424-03-2P
570424-04-3P 570424-05-4P 570424-06-5P 570424-07-6P
571206-22-9P 571206-26-3P 571206-45-6P 571206-47-8P
571206-49-0P 571206-50-3P 571206-51-4P 571206-52-5P
571206-53-6P 571206-54-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of amino functionalized organo phosphonates or organo
carboxylates as S1P1/Edg1 receptor
agonists)

SEARCH

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=> => d his l119

     (FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007)
L119            0 S L117 NOT L101

=> d que l119
L2            424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
                  101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
                  103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
                  106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
                  110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
                  1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
                  121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
                  130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
                  13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
                  13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
                  146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
                  15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
                  17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
                  19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
                  208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
                  2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
                  24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
                  2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
                  2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
                  2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
                  3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
                  3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
                  35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
                  38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
                  40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
                  4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
                  49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
                  50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
                  54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
                  54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
                  7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
                  I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
                   OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
                  OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
                  OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
                  OR 569682-80-0/BI OR 569682-81-1/BI OR 569
L3             71 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/NR AND 1/P
                  AND 1/N
L4            154 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/P
L6             23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND C4N/RF
L8             36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
L9             67 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4N/RF
L10             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND L9
L11             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L11
L13            43 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 3/F
L14            36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L8
L15             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L10
L16            12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C3N/RF
L17             6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L8
L18             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L11
L19            40 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND C6/RF AND
                  2/NR
L20             9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L19 AND 4/O
L21             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L20 AND C22 H33 N
                  O4/MF
L22             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 1/F
L23             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND 2/NR AND 2/O
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L24          22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 2/NR AND
                2-3/O AND C6/RF
L25          11 SEA FILE=REGISTRY ABB=ON  PLU=ON  L24 AND 2/O
L26           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L25 AND 21/C
L27           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L24 AND 20/C AND 3/O

L28           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 2/BR
L29           3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L28 AND 2/NR
L30           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 2/NR AND 5/O
                AND 1/P
L31           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND 4/NR
L32           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L31 AND 3/O
L33          27 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND 4/O
L34          10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
L35           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND 20-30/C
L37          44 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?BIPHENYL?/CNS

L38          32 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND 20-100/C
L41          68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND C6/RF
L42          68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 AND 12-50/C
L43         157 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR (L10 OR L11 OR
                L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19
                OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR
                L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35
                OR L38
L44         199 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L41 OR L42 OR L43)
L48             QUE  ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
                MY<2003 OR REVIEW/DT
L50             QUE  ABB=ON  PLU=ON  IMMUNOSUPPRES? OR IMMUNOREG? OR IM
                MUN?(A)(SUPPRESS? OR REG?)
L52             QUE  ABB=ON  PLU=ON  IMMUNOSUPPRESSANTS+PFT,OLD,NT/CT
L53             QUE  ABB=ON  PLU=ON  IMMUNOSUPPRESSION+PFT,OLD,NT/CT
L55             QUE  ABB=ON  PLU=ON  ANTAGONISM+PFT,OLD,NT/CT
L57             QUE  ABB=ON  PLU=ON  AGON? OR ANTAG?
L59             QUE  ABB=ON  PLU=ON  EDG1(A)S1P?
L70             QUE  ABB=ON  PLU=ON  "AUTOIMMUNE DISEASE"+PFT,OLD,NT/CT
L72             QUE  ABB=ON  PLU=ON  INFLAMMATION+PFT,OLD,NT/CT
L74             QUE  ABB=ON  PLU=ON  INFECTION+PFT,OLD,NT/CT
L76             QUE  ABB=ON  PLU=ON  AIDS+PFT,OLD,NT/CT
L78             QUE  ABB=ON  PLU=ON  ASTHMA+PFT,OLD,NT/CT
L80             QUE  ABB=ON  PLU=ON  "RESPIRATORY SYSTEM, DISEASE"+PFT,
                OLD,NT/CT
L82             QUE  ABB=ON  PLU=ON  ARTHRITIS+PFT,OLD,NT/CT
L84             QUE  ABB=ON  PLU=ON  "MUSCULAR DYSTROPHY"+PFT,OLD,NT/CT
L86             QUE  ABB=ON  PLU=ON  "SKIN, DISEASE"+PFT,OLD,NT/CT
L88             QUE  ABB=ON  PLU=ON  DERMATITIS+PFT,OLD,NT/CT
L94             QUE  ABB=ON  PLU=ON  NEOPLASM+PFT,OLD,NT/CT
L97        1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
                A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
                AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
                "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
                "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98             QUE  ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99          714 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L48
L100         228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99 AND L98
L101          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L50
L105         179 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 AND 18-70/C
L106          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L105
L109          20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 NOT L105
L110           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C14 H24 N
                O4 P/MF
L111           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C17 H29 BR
                N O5 P/MF
L112         181 SEA FILE=REGISTRY ABB=ON  PLU=ON  L105 OR L110 OR L111

L113          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L112
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L114          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L106 OR L113
L115           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L114 AND L48
L116           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L115 AND (L50 OR (L52
                 OR L53) OR L55 OR L57 OR L59 OR L70 OR L72 OR L74 OR
                 L76 OR L78 OR L80)
L117           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L116 AND (L82 OR L84
                 OR L86 OR L88 OR L94)
L119           0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L117 NOT L101


=> d his l121

     (FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007)
L121           0 S L120 NOT L101

=> d que l121
L2           424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
                 101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
                 103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
                 106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
                 110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
                 1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
                 121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
                 130592-02-8/BI OR 131138-33-5/BI OR 131888-48-7/BI OR
                 13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
                 13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
                 146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
                 15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
                 17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
                 19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
                 208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
                 2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
                 24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
                 2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
                 2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
                 2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
                 3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
                 3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
                 35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
                 38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
                 40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
                 4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
                 49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
                 50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
                 54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
                 54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
                 7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
                 I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
                  OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
                 OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
                 OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
                 OR 569682-80-0/BI OR 569682-81-1/BI OR 569
L3            71 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/HR AND 1/P
                 AND 1/N
L4           154 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/P
L6            23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND C4N/RF
L8            36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
L9            67 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4N/RF
L10            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND L9
L11            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L11
L13           43 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 3/F
L14           36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L8
L15            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L10
L16           12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C3N/RF
L17            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L8
L18            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L11
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L19          40 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND C6/RF AND
                2/NR
L20           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L19 AND 4/O
L21           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L20 AND C22 H33 N
                O4/MF
L22           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 1/F
L23           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND 2/NR AND 2/O

L24          22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 2/NR AND
                2-3/O AND C6/RF
L25          11 SEA FILE=REGISTRY ABB=ON  PLU=ON  L24 AND 2/O
L26           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L25 AND 21/C
L27           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L24 AND 20/C AND 3/O

L28           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 2/BR
L29           3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L28 AND 2/NR
L30           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 2/NR AND 5/O
                AND 1/P
L31           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND 4/NR
L32           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L31 AND 3/O
L33          27 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND 4/O
L34          10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
L35           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND 20-30/C
L37          44 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?BIPHENYL?/CNS

L38          32 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND 20-100/C
L41          68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND C6/RF
L42          68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 AND 12-50/C
L43         157 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR (L10 OR L11 OR
                L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19
                OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR
                L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35
                OR L38
L44         199 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L41 OR L42 OR L43)
L45         849 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44
                QUE  ABB=ON  PLU=ON  PHARMAC?/SC,SX
L47         483 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND L46
L48             QUE  ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
                MY<2003 OR REVIEW/DT
L49         270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L47 AND L48
L50             QUE  ABB=ON  PLU=ON  IMMUNOSUPPRES? OR IMMUNOREG? OR IM
                MUN?(A)(SUPPRESS? OR REG?)
L51           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L50
L60          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  EDG1(A)S1P?
L61           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L60 AND L49
L68             QUE  ABB=ON  PLU=ON  AUTOIMMUN?
L69          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L68
L70             QUE  ABB=ON  PLU=ON  "AUTOIMMUNE DISEASE"+PFT,OLD,NT/CT
L71          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L70
L72             QUE  ABB=ON  PLU=ON  INFLAMMATION+PFT,OLD,NT/CT
L73          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L72
L74             QUE  ABB=ON  PLU=ON  INFECTION+PFT,OLD,NT/CT
L75          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L74
L76             QUE  ABB=ON  PLU=ON  AIDS+PFT,OLD,NT/CT
L77           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L76
L78             QUE  ABB=ON  PLU=ON  ASTHMA+PFT,OLD,NT/CT
L79          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L78
L80             QUE  ABB=ON  PLU=ON  "RESPIRATORY SYSTEM, DISEASE"+PFT,
                OLD,NT/CT
L81          29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L80
L82             QUE  ABB=ON  PLU=ON  ARTHRITIS+PFT,OLD,NT/CT
L83          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L82
L84             QUE  ABB=ON  PLU=ON  "MUSCULAR DYSTROPHY"+PFT,OLD,NT/CT
L85           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L84
L86             QUE  ABB=ON  PLU=ON  "SKIN, DISEASE"+PFT,OLD,NT/CT
L87          30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L86
L88             QUE  ABB=ON  PLU=ON  DERMATITIS+PFT,OLD,NT/CT
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L89          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L88
L90          68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 OR L61 OR L69 OR
                L71 AND L73 OR L75 OR L77 OR L79 OR L81 OR L83 OR L85
                OR L89 OR L87
L94              QUE  ABB=ON  PLU=ON  NEOPLASM+PFT,OLD,NT/CT
L95          44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L94
L96          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L90
L97        1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
                A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
                AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
                "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
                "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98              QUE  ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99         714 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L48
L100        228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99 AND L98
L101         26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L50
L120          4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L50
L121          0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L120 NOT L101


=> d his l122

     (FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007)
L122         12 S L113 NOT (L118 OR L120)

=> d que l122
L2          424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
                101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
                103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
                106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
                110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
                1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
                121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
                130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
                13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
                13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
                146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
                15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
                17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
                19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
                208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
                2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
                24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
                2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
                2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
                2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
                3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
                3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
                35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
                38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
                40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
                4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
                49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
                50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
                54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
                54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
                7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
                I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
                 OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
                OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
                OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
                OR 569682-80-0/BI OR 569682-81-1/BI OR 569
L3           71 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/NR AND 1/P
                AND 1/N
L4          154 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/P
L6           23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND C4N/RF
L8           36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
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L9          67 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4N/RF
L10          7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND L9
L11          7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L11
L13         43 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 3/F
L14         36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L8
L15          7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L10
L16         12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C3N/RF
L17          6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L8
L18          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L11
L19         40 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND C6/RF AND
               2/NR
L20          9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L19 AND 4/O
L21          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L20 AND C22 H33 N
               O4/MF
L22          2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 1/F
L23          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND 2/NR AND 2/O

L24         22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 2/NR AND
               2-3/O AND C6/RF
L25         11 SEA FILE=REGISTRY ABB=ON  PLU=ON  L24 AND 2/O
L26          2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L25 AND 21/C
L27          4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L24 AND 20/C AND 3/O

L28          6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 2/BR
L29          3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L28 AND 2/NR
L30          6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 2/NR AND 5/O
               AND 1/P
L31          6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND 4/NR
L32          5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L31 AND 3/O
L33         27 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND 4/O
L34         10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
L35          5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND 20-30/C
L37         44 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?BIPHENYL?/CNS

L38         32 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND 20-100/C
L41         68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND C6/RF
L42         68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 AND 12-50/C
L43        157 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR (L10 OR L11 OR
               L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19
               OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR
               L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35
               OR L38
L44        199 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L41 OR L42 OR L43)
L45        849 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44
L46            QUE  ABB=ON  PLU=ON  PHARMAC?/SC,SX
L47        483 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND L46
L48            QUE  ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
               MY<2003 OR REVIEW/DT
L49        270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L47 AND L48
L50            QUE  ABB=ON  PLU=ON  IMMUNOSUPPRES? OR IMMUNOREG? OR IM
               MUN?(A)(SUPPRESS? OR REG?)
L51          7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L50
L52            QUE  ABB=ON  PLU=ON  IMMUNOSUPPRESSANTS+PFT,OLD,NT/CT
L53            QUE  ABB=ON  PLU=ON  IMMUNOSUPPRESSION+PFT,OLD,NT/CT
L55            QUE  ABB=ON  PLU=ON  ANTAGONISM+PFT,OLD,NT/CT
L57            QUE  ABB=ON  PLU=ON  AGON? OR ANTAG?
L59            QUE  ABB=ON  PLU=ON  EDG1(A)S1P?
L60         19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  EDG1(A)S1P?
L61          2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L60 AND L49
L68            QUE  ABB=ON  PLU=ON  AUTOIMMUN?
L69         21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L68
L70            QUE  ABB=ON  PLU=ON  "AUTOIMMUNE DISEASE"+PFT,OLD,NT/CT
L71         32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L70
L72            QUE  ABB=ON  PLU=ON  INFLAMMATION+PFT,OLD,NT/CT
L73         41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L72
L74            QUE  ABB=ON  PLU=ON  INFECTION+PFT,OLD,NT/CT
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L75          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L74
L76             QUE  ABB=ON  PLU=ON  AIDS+PFT,OLD,NT/CT
L77           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L76
L78             QUE  ABB=ON  PLU=ON  ASTHMA+PFT,OLD,NT/CT
L79          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L78
L80             QUE  ABB=ON  PLU=ON  "RESPIRATORY SYSTEM, DISEASE"+PFT,
                OLD,NT/CT
L81          29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L80
L82             QUE  ABB=ON  PLU=ON  ARTHRITIS+PFT,OLD,NT/CT
L83          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L82
L84             QUE  ABB=ON  PLU=ON  "MUSCULAR DYSTROPHY"+PFT,OLD,NT/CT
L85           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L84
L86             QUE  ABB=ON  PLU=ON  "SKIN, DISEASE"+PFT,OLD,NT/CT
L87          30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L86
L88             QUE  ABB=ON  PLU=ON  DERMATITIS+PFT,OLD,NT/CT
L89          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L88
L90          68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 OR L61 OR L69 OR
                L71 AND L73 OR L75 OR L77 OR L79 OR L81 OR L83 OR L85
                OR L89 OR L87
L94             QUE  ABB=ON  PLU=ON  NEOPLASM+PFT,OLD,NT/CT
L95          44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L94
L96          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L90
L97        1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
                A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
                AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEHU"/AU OR
                "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
                "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98             QUE  ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99         714 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L48
L100        228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99 AND L98
L101         26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L50
L103         28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 NOT L101
L105        179 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 AND 18-70/C
L106         15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L105
L109         20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 NOT L105
L110          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C14 H24 N
                O4 P/MF
L111          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C17 H29 BR
                N O5 P/MF
L112        181 SEA FILE=REGISTRY ABB=ON  PLU=ON  L105 OR L110 OR L111

L113         15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L112
L114         15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L106 OR L113
L115          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L114 AND L48
L116          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L115 AND (L50 OR (L52
                OR L53) OR L55 OR L57 OR L59 OR L70 OR L72 OR L74 OR
                L76 OR L78 OR L80)
L117          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L116 AND (L82 OR L84
                OR L86 OR L88 OR L94)
L118          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L117 NOT L103
L120          4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L50
L122         12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L113 NOT (L118 OR
                L120)


=> d his l127

     (FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 12:40:59 ON 27
     JUL 2007)
L127          0 S L126

=> d que l127
L2          424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
                101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
                103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
                106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
                110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
```

1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
OR 569682-80-0/BI OR 569682-81-1/BI OR 569

| | | |
|---|---|---|
| L3 | 71 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND 1/NR AND 1/P AND 1/N |
| L4 | 154 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND 1/P |
| L6 | 23 | SEA FILE=REGISTRY ABB=ON PLU=ON L4 AND C4N/RF |
| L8 | 36 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C4S/RF |
| L9 | 67 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C4N/RF |
| L10 | 7 | SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND L9 |
| L11 | 7 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C2N2O/RF |
| L12 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND L11 |
| L13 | 43 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND 3/F |
| L14 | 36 | SEA FILE=REGISTRY ABB=ON PLU=ON L13 AND L8 |
| L15 | 7 | SEA FILE=REGISTRY ABB=ON PLU=ON L13 AND L10 |
| L16 | 12 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C3N/RF |
| L17 | 6 | SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND L8 |
| L18 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND L11 |
| L19 | 40 | SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND C6/RF AND 2/NR |
| L20 | 9 | SEA FILE=REGISTRY ABB=ON PLU=ON L19 AND 4/O |
| L21 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON L20 AND C22 H33 N O4/MF |
| L22 | 2 | SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND 1/F |
| L23 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND 2/NR AND 2/O |
| L24 | 22 | SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND 2/NR AND 2-3/O AND C6/RF |
| L25 | 11 | SEA FILE=REGISTRY ABB=ON PLU=ON L24 AND 2/O |
| L26 | 2 | SEA FILE=REGISTRY ABB=ON PLU=ON L25 AND 21/C |
| L27 | 4 | SEA FILE=REGISTRY ABB=ON PLU=ON L24 AND 20/C AND 3/O |
| L28 | 6 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND 2/BR |
| L29 | 3 | SEA FILE=REGISTRY ABB=ON PLU=ON L28 AND 2/NR |
| L30 | 6 | SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND 2/NR AND 5/O AND 1/P |
| L31 | 6 | SEA FILE=REGISTRY ABB=ON PLU=ON L15 AND 4/NR |
| L32 | 5 | SEA FILE=REGISTRY ABB=ON PLU=ON L31 AND 3/O |
| L33 | 27 | SEA FILE=REGISTRY ABB=ON PLU=ON L3 AND 4/O |

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L34          10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
L35           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND 20-30/C
L37          44 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?BIPHENYL?/CNS

L38          32 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND 20-100/C
L41          68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND C6/RF
L42          68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 AND 12-50/C
L43         157 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR (L10 OR L11 OR
                L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19
                OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR
                L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35
                OR L38
L44         199 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L41 OR L42 OR L43)
L105        179 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 AND 18-70/C
L109         20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 NOT L105
L110          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C14 H24 N
                O4 P/MF
L111          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C17 H29 BR
                N O5 P/MF
L112        181 SEA FILE=REGISTRY ABB=ON  PLU=ON  L105 OR L110 OR L111

L126          0 SEA FILE=REGISTRY ABB=ON  PLU=ON  L112 AND EMBASE/LC
L127          0 SEA L126


=> dup rem l119 l121 l122 l127
L119 HAS NO ANSWERS
L121 HAS NO ANSWERS
L127 HAS NO ANSWERS
FILE 'HCAPLUS' ENTERED AT 13:06:51 ON 27 JUL 2007
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PROCESSING COMPLETED FOR L119
PROCESSING COMPLETED FOR L121
PROCESSING COMPLETED FOR L122
PROCESSING COMPLETED FOR L127
L134         12 DUP REM L119 L121 L122 L127 (0 DUPLICATES REMOVED)
                ANSWERS '1-12' FROM FILE HCAPLUS
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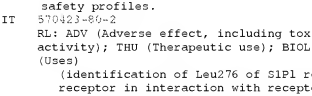
SEARCH RESULTS

=> d l134 1-12 ibib ed abs hitstr hitind

L134 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:262972 HCAPLUS Full-text
DOCUMENT NUMBER: 146:474760
TITLE: Identification of Leu276 of the S1P1 receptor and Phe263 of the S1P3 receptor in interaction with receptor specific agonists by molecular modeling, site-directed mutagenesis, and affinity studies
AUTHOR(S): Deng, Qiaolin; Clemas, Joseph A.; Chrebet, Gary; Fischer, Paul; Hale, Jeffrey J.; Li, Zhen; Mills, Sander G.; Bergstrom, James; Mandala, Suzanne; Mosley, Ralph; Parent, Stephen A.
CORPORATE SOURCE: Department of Molecular Systems, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Molecular Pharmacology (2007), 71(3), 724-735
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Mar 2007
AB Sphingosine-1-phosphate (S1P) receptor agonists are novel immunosuppressive agents. The selectivity of S1P1 against S1P3 is strongly correlated with lymphocyte sequestration and min. acute toxicity and bradycardia. This study describes mol. modeling, site-directed mutagenesis, and affinity studies exploring the mol. basis for selectivity between S1P1 and S1P3 receptors. Computational models of human S1P1 and S1P3 receptors bound with two nonselective agonists or two S1P1-selective agonists were developed based on the x-ray crystal structure of bovine rhodopsin. The models predict that S1P1 Leu276 and S1P3 Phe263 contribute to the S1P1/S1P3 selectivity of the two S1P1-selective agonists. These residues were subjected to site-directed mutagenesis. The wild-type and mutant S1P receptors were expressed in Chinese hamster ovary cells and examined for their abilities to bind to and be activated by agonists in vitro. The results indicate that the mutations have minimal effects on the activities of the two nonselective agonists, although they have dramatic effects on the S1P1-selective agonists. These studies provide a fundamental understanding of how these two receptor-selective agonists bind to the S1P1 and S1P3 receptors, which should aid development of more selective S1P1 receptor agonists with immunosuppressive properties and improved safety profiles.
IT 570423-80-2
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of Leu276 of S1P1 receptor and Phe263 of S1P3 receptor in interaction with receptor specific agonists by mol. modeling, site-directed mutagenesis, and affinity studies)
RN 570423-80-2 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)




CC 1-3 (Pharmacology)
IT 26993-30-6, Sphingosine 1-phosphate 162359-56-0, FTY720

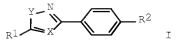
402615-91-2, FTY720-P 570423-89-2 635701-59-6
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of Leu276 of S1P1 receptor and Phe263 of S1P3 receptor in interaction with receptor specific agonists by mol. modeling, site-directed mutagenesis, and affinity studies)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1311129 HCAPLUS Full-text
DOCUMENT NUMBER: 146:62699
TITLE: Preparation of polycyclic oxadiazoles or isoxazoles as S1P receptor ligands
INVENTOR(S): Albert, Rainer; Weiler, Sven; Zecri, Frederic
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 53pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

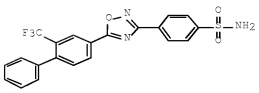
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006131336 | A1 | 20061214 | WO 2006-EP5422 | 20060607 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| GB 2005-11684 | A | 20050608 |
| GB 2005-25064 | A | 20051208 |
| GB 2006-405 | A | 20060110 |

OTHER SOURCE(S): MARPAT 146:62699
ED Entered STN: 15 Dec 2006
GI



I



II

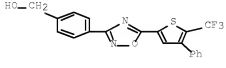
AB Title compds. represented by the formula I [wherein X = -N=, Y = O; X = -O-, Y = -N=; R1 = substituted biphenyl, 4-phenoxyphenyl or 4-(phenylalkoxy)phenyl; R2 = (un)substituted alkyl, amino, sulfamoyl, etc.; and physiol. hydrolyzable derivs., hydrates or solvates thereof] were prepared as sphingosine-1-phosphate (S1P) receptor ligands. For example, II was provided in a multi-step synthesis starting from 4-chloro-3-trifluoromethylbenzoic acid. I showed binding affinity to human S1P1 receptor with EC50 < 1 nM, are active in in vitro FLIPR calcium flux assay at a concentration of from 10-12-3.10-5 nM, and have EC50 of less than 10 mg/kg in in vivo screening assays for measurement of blood lymphocyte depletion. Thus, I and their pharmaceutical compns. are useful as S1P receptor ligands, particularly as immunosuppressants.

IT 569685-50-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polycyclic oxadiazoles or isoxazoles as S1P receptor ligands)

RN 569685-50-3 HCAPLUS

CN Benzenemethanol, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]- (CA INDEX NAME)



CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 569685-50-3P 916804-38-1P 916804-44-9P 916804-47-2P
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916804-77-8P 916804-85-8P 916804-91-6P 916804-98-3P
916805-01-1P 916805-05-5P 916805-07-7P 916805-09-9P
916805-11-3P 916805-13-5P 916805-15-7P 916805-16-8P
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916806-80-9P 916806-81-0P 916806-82-1P 916806-83-2P
916806-84-3P 916806-85-4P 916833-78-8P 916833-79-9P
916833-80-2P 916833-81-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polycyclic oxadiazoles or isoxazoles as S1P receptor ligands)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:818237 HCAPLUS Full-text
DOCUMENT NUMBER: 145:224859
TITLE: Antilymphocyte antibody induction for prevention of transplant rejection
INVENTOR(S): Aradhye, Shreeram
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006086361 | A2 | 20060817 | WO 2006-US4234 | 20060206 |
| WO 2006086361 | A3 | 20070118 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-651045P P 2005 0208

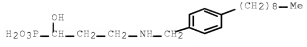
ED Entered STN: 17 Aug 2006

AB An immunosuppressive treatment combining a S1P receptor modulator, one or more immunosuppressive drug(s) and an antilymphocyte antibody in the course of the treatment of a transplant recipient prolongs the survival of a transplant allograft. Thus, the patients were administered (i) FTY720 5 mg given 2 to 12 h prior to renal allograft revascularization, then 2.5 mg daily, (ii) cyclosporine A 8 to 10 mg/kg/day adjusted to achieve target blood levels, and (iii) corticosteroids. The dosage regimen of the study had a beneficial effect compared to standard immunosuppressive regimens.

IT 569684-46-4 569684-82-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte antibody in combination with immunosuppressant and S1P receptor modulator for prevention of transplant rejection)

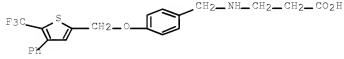
RN 569684-46-4 HCAPLUS

CN Phosphonic acid, [1-hydroxy-3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)




RN 569684-82-8 HCAPLUS

CN β-Alanine, N-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)




CC 1-7 (Pharmacology)
Section cross-reference(s): 15, 63

IT 24280-93-1, Mycophenolic acid 59865-13-3, Cyclosporine A 162359-56-0, FTY 720 569684-46-4 569684-82-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte antibody in combination with immunosuppressant and S1P receptor modulator for prevention of transplant rejection)

L134 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:677741 HCAPLUS Full-text

DOCUMENT NUMBER: 145:117363

TITLE: Use of sphingosine-1-phosphate (S1P) receptor agonists for the treatment of hepatitis C virus (HCV) disorders

INVENTOR(S): Brinkmann, Volker; Feutren, Gilles

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH

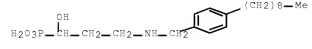
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006072562 | A1 | 20060713 | WO 2006-EP3 | 2006 0102 |

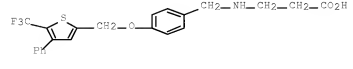
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-20 A 2005 0104

OTHER SOURCE(S): MARPAT 145:117363
ED Entered STN: 13 Jul 2006
AB S1P receptor agonists are useful for the treatment of hepatitis C or chronic hepatitis C (HCV).
IT 569684-46-4 569684-82-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S1P receptor agonists for treatment of hepatitis C virus disorders)
RN 569684-46-4 HCAPLUS
CN Phosphonic acid, [1-hydroxy-3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)




RN 569684-82-8 HCAPLUS
CN β-Alanine, N-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

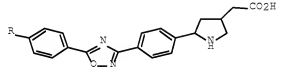



CC 1-5 (Pharmacology)
IT 569684-46-4 569684-82-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S1P receptor agonists for treatment of hepatitis C virus disorders)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:499151 HCAPLUS Full-text
DOCUMENT NUMBER: 145:145483
TITLE: 2-Aryl(pyrrolidin-4-yl)acetic acids are potent agonists of sphingosine-1-phosphate (S1P) receptors
AUTHOR(S): Yan, Lin; Budhu, Richard; Huo, Pei; Lynch, Christopher L.; Hale, Jeffrey J.; Mills, Sander G.; Hajdu, Richard; Keohane, Carol A.; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Mandala, Suzanne M.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(13), 3564-3568
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:145483
ED Entered STN: 29 May 2006
GI

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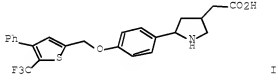
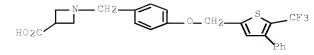



II

AB 2-Aryl(pyrrolidin-4-yl)acetic acids I [R = i-Bu, cyclopentyl, cyclohexyl, F3C(CH2)2, 3,3-difluoro-1-cyclopentyl, 4,4-difluoro-1-cyclohexyl] and II were synthesized and their biol. activities as agonists of S1P receptors were evaluated. These analogs were able to induce lowering of lymphocyte counts in the peripheral blood of mice and were found to have good overall pharmacokinetic properties in rats.

IT 570423-67-5
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(preparation and biol. activity of thiophene- or oxadiazole-functionalized (aryl)pyrrolidineacetic acids as potent agonists of sphingosine-1-phosphate receptors)

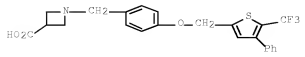
RN 570423-67-5 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28
IT 570423-67-5 635701-59-6
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(preparation and biol. activity of thiophene- or oxadiazole-functionalized (aryl)pyrrolidineacetic acids as potent agonists of sphingosine-1-phosphate receptors)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

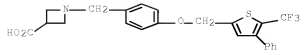
L134 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:772794 HCAPLUS Full-text
DOCUMENT NUMBER: 145:369215
TITLE: Species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist in rats and dogs: formation of a unique glutathione adduct in the rat
AUTHOR(S): Anari, M. Reza; Creighton, Mellissa D.; Ngui, Jason S.; Tschirret-Guth, Richard A.; Teffera, Yohannes; Doss, George A.; Tang, Wei; Yu, Nathan X.; Ciccotto, Suzanne L.; Hobra, Donald F., Jr.; Coleman, John B.; Vincent, Stella H.; Evans, David C.
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, USA
SOURCE: Drug Metabolism and Disposition (2006), 34(8), 1367-1375
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Aug 2006
AB The pharmacokinetics and metabolism of 1-(4-((4-phenyl-5- trifluoromethyl-2-thienyl)methoxy)benzyl)azetidine-3-carboxylic acid (MRL-A), a selective agonist for the sphingosine-1-phosphate 1 (S1P1) receptor, were investigated in rats and dogs. In both species, more than 50% of the dose was excreted in bile. Specific to the rat, and observed in bile, were a taurine conjugate of MRL-A and a glucuronide conjugate of an azetidine lactam metabolite. In dogs, a smaller portion of the dose (54% of administered dose) was excreted intact in bile, and the major metabolites detected were an azetidine N-oxide of MRL-A and an acylglucuronide of an N-dealkylation product. This latter metabolite was also observed in rat bile. Stereoselective formation of the N-oxide isomer was observed in dogs, whereas the rat produced comparable amts. of both isomers. The formation of a unique glutathione adduct was observed in rat bile, which was proposed to occur via N-dealkylation, followed by reduction of the putative aldehyde product to form the alc., and dehydration of the alc. to generate a reactive quinone methide intermediate. Incubation of a synthetic standard of this alc. in rat microsomes fortified with reduced glutathione or rat hepatocytes resulted in formation of this unique glutathione adduct.
IT 570423-67-5, MRL-A
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
RN 570423-67-5 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-

thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

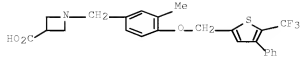


CC 1-2 (Pharmacology)
IT 570423-67-5, MRL-A
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:986123 HCAPLUS Full-text
DOCUMENT NUMBER: 143:431986
TITLE: Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity against S1P2 and S1P3
AUTHOR(S): Li, Zhen; Chen, Weirong; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Chrebet, Gary; Parent, Stephen A.; Bergstrom, James; Card, Deborah; Forrest, Michael; Quackenbush, Elizabeth J.; Wickham, L. Alexandra; Vargas, Hugo; Evans, Rose M.; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Departments of Medicinal Chemistry and Immunology Rheumatology Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(20), 6169-6173
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:431986
ED Entered STN: 11 Sep 2005
AB A class of 3,5-diphenyl-1,2,4-oxadiazole based compds. have been identified as potent sphingosine-1-phosphate-1 (S1P1) receptor agonists with minimal affinity for the S1P2 and S1P3 receptor subtypes. Analog 26 (S1P1 IC50 = 0.6 nM) has an excellent pharmacokinetics profile in the rat and dog and is efficacious in a rat skin transplant model, indicating that S1P3 receptor agonism is not a component of immunosuppressive efficacy.
IT 570423-67-5 570423-80-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity)
RN 570423-67-5 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

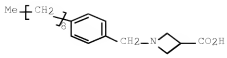


RN 570423-80-2 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



CC 1-3 (Pharmacology)
Section cross-reference(s): 28
IT 159222-57-8 162359-55-9 402615-91-2 570423-67-5 570423-80-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1048937 HCAPLUS Full-text
DOCUMENT NUMBER: 142:147835
TITLE: A Rational Utilization of High-Throughput Screening Affords Selective, Orally Bioavailable 1-Benzyl-3-carboxyazetidine Sphingosine-1-phosphate-1 Receptor Agonists
AUTHOR(S): Hale, Jeffrey J.; Lynch, Christopher L.; Neway, William; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Parent, Stephen A.; Chrebet, Gary; Bergstrom, James; Card, Deborah; Ferrer, Marc; Hodder, Peter; Strulovici, Berta; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Departments of Medicinal Chemistry and Immunology and Rheumatology Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(27), 6662-6665
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:147835
ED Entered STN: 08 Dec 2004
GI

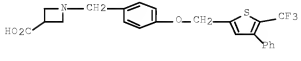


I

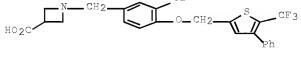
AB Moderately potent, selective S1P1 receptor agonists identified from high-throughput screening have been adapted into lipophilic tails for a class of orally bioavailable amino acid-based S1P1 agonists represented by I. Many of the new compds. are potent S1P1 agonists that select against the S1P2, S1P3, and S1P4 (although not S1P5) receptor subtypes. Two of the analogs are highly orally bioavailable and possess excellent pharmacokinetic profiles in the rat, dog, and rhesus monkey.

IT 570423-67-5P 570423-76-6P 570423-80-2P
570423-81-3P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

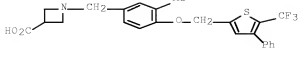
RN 570423-67-5 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



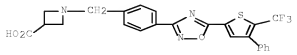
RN 570423-76-6 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



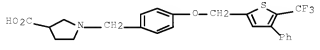
RN 570423-80-2 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



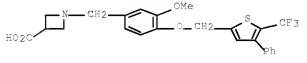
RN 570423-81-3 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)



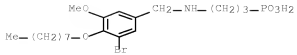
IT 570423-45-9P 570423-78-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)
RN 570423-45-9 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



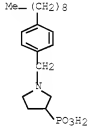
RN 570423-78-8 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



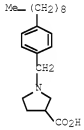
IT 569683-55-2 570423-38-0 570423-46-0 570423-68-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)
RN 569683-55-2 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



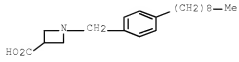
RN 570423-38-0 HCAPLUS
CN Phosphonic acid, [1-[(4-nonylphenyl)methyl]-3-pyrrolidinyl]- (9CI)
(CA INDEX NAME)



RN 570423-46-0 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[(4-nonylphenyl)methyl]- (9CI)
(CA INDEX NAME)



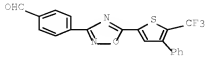
RN 570423-68-6 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[(4-nonylphenyl)methyl]- (9CI) (CA
INDEX NAME)



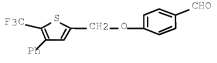
IT 569685-42-3P 569685-43-4P 569685-49-0P
569685-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists
and immunosuppressants: high-throughput screening for oral

bioavailability and preparation)

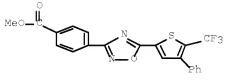
RN 569685-42-3 HCAPLUS
CN Benzaldehyde, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



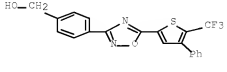
RN 569685-43-4 HCAPLUS
CN Benzaldehyde, 4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]- (9CI) (CA INDEX NAME)



RN 569685-49-0 HCAPLUS
CN Benzoic acid, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]-, methyl ester (9CI) (CA INDEX NAME)



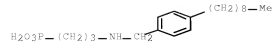
RN 569685-50-3 HCAPLUS
CN Benzenemethanol, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]- (CA INDEX NAME)



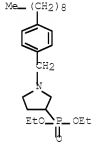
CC 1-3 (Pharmacology)
Section cross-reference(s): 27
IT 570423-67-5P 570423-78-6P 570423-80-2P
570423-81-3P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral

bioavailability and preparation)
IT 570423-45-9P 570423-78-8P 828269-16-5P
828269-17-6P 828269-18-7P 828269-19-8P 828269-20-1P
828269-21-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)
IT 162359-56-0, FTY 720 256414-75-2 256414-76-3 256414-81-0
402615-91-2 569683-55-2 570423-38-0
570423-46-0 570423-68-6 725724-60-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)
IT 146936-34-7P 167279-18-7P 208108-76-3P 256488-46-7P
569685-42-3P 569685-43-4P 569685-49-0P
569685-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

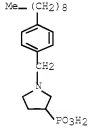
L134 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:729837 HCAPLUS Full-text
DOCUMENT NUMBER: 141:395611
TITLE: Design and synthesis of conformationally constrained 3-(N-alkylamino)propylphosphonic acids as potent agonists of sphingosine-1-phosphate (S1P) receptors
AUTHOR(S): Yan, Lin; Hale, Jeffrey J.; Lynch, Christopher L.; Budhu, Richard; Gentry, Amy; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Rosen, Hugh; Mandala, Suzanne M.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(19), 4861-4866
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:395611
ED Entered STN: 08 Sep 2004
AB Conformationally constrained 3-(N-alkylamino)propylphosphonic acids were systematically synthesized and their activities as S1P receptor agonists were evaluated. Several pyrrolidine and cyclohexane analogs had S1P receptor profiles comparable to the acyclic lead compound, 3-(N-tetradecylamino)propylphosphonic acid (3), lowered circulating lymphocytes in mice after iv administration and were thus identified as being suitable for further studies.
IT 569684-50-0
RL: PAC (Pharmacological activity); BIOL (Biological study)
(design and synthesis of conformationally constrained (alkylamino)propylphosphonic acids as potent agonists of sphingosinephosphate (S1P) receptors)
RN 569684-50-0 HCAPLUS
CN Phosphonic acid, [3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



IT 570423-96-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and synthesis of conformationally constrained (alkylamino)propylphosphonic acids as potent agonists of sphingosinephosphate (S1P) receptors)
RN 570423-96-0 HCAPLUS
CN Phosphonic acid, [1-[(4-nonylphenyl)methyl]-3-pyrrolidinyl]-, diethyl ester (9CI) (CA INDEX NAME)



IT 570423-38-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of alkylpyrrolidinylphosphonate as conformationally constrained (alkylamino)propylphosphonic acids useful as potent agonists of sphingosinephosphate (S1P) receptors)
RN 570423-38-0 HCAPLUS
CN Phosphonic acid, [1-[(4-nonylphenyl)methyl]-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)



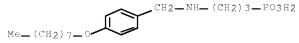
CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1
IT 402615-91-2 569684-50-0 725724-60-7 785815-68-1
RL: PAC (Pharmacological activity); BIOL (Biological study)
(design and synthesis of conformationally constrained (alkylamino)propylphosphonic acids as potent agonists of

sphingosinephosphate (S1P) receptors)
IT 17012-21-4P 157634-00-9P 570423-92-6P 570423-96-0P
849811-77-4P 849811-93-4P 849811-94-5P 849812-00-6P
849812-20-0P 849812-22-2P 849812-30-2P 849812-61-9P
849813-76-9P 849813-78-1P 849813-85-0P 849813-86-1P
849813-88-3P 849814-14-8P 849814-16-0P 849814-18-2P
849814-20-6P 849814-22-8P 849814-23-9P 849815-30-1P
849816-37-1P 849816-38-2P 849816-39-3P 849816-43-9P
849816-44-0P 849816-48-4P 849816-51-9P 849816-84-8P
849817-15-8P 849817-72-7P 849818-04-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and synthesis of conformationally constrained (alkylamino)propylphosphonic acids as potent agonists of sphingosinephosphate (S1P) receptors)
IT 570423-38-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of alkylpyrrolidinylphosphonate as conformationally constrained (alkylamino)propylphosphonic acids useful as potent agonists of sphingosinephosphate (S1P) receptors)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:465500 HCAPLUS Full-text
DOCUMENT NUMBER: 141:116457
TITLE: Selecting against S1P3 enhances the acute cardiovascular tolerability of 3-(N-benzyl)aminopropylphosphonic acid S1P receptor agonists
AUTHOR(S): Hale, Jeffrey J.; Doherty, George; Toth, Leslie; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark; Milligan, James; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Forrest, Michael; Sun, Shu-Yu; West, Sarah; Xie, Huijuan; Nomura, Naomi; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(13), 3501-3505
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:116457
ED Entered STN: 10 Jun 2004
AB Structurally modified 3-(N-benzylamino)propylphosphonic acid S1P receptor agonists that maintain affinity for S1P1, and have decreased affinity for S1P3 are efficacious, but exhibit decreased acute cardiovascular toxicity in rodents compared to nonselective agonists.
IT 569682-67-7P 569682-68-8P 569682-73-1P
569682-91-3P 569682-93-5P 569682-97-9P
569683-93-1P 569683-61-8P 569683-30-3P
569683-32-5P 569683-34-7P 569683-55-2P
569683-58-5P 569683-61-0P 569683-63-2P
569683-70-1P 569683-76-7P 569683-78-9P
569683-81-4P 569683-82-5P 569683-89-2P
569683-90-5P 569683-92-7P 569684-01-1P
569684-22-8P 569684-50-0P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(selecting against S1P3 enhances acute cardiovascular tolerability of 3-(N-benzyl)aminopropylphosphonic acid S1P

receptor agonists)

RN 569682-67-3 HCAPLUS
CN Phosphonic acid, [3-[[[4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569682-68-4 HCAPLUS
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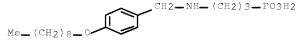

RN 569682-73-1 HCAPLUS
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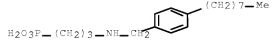
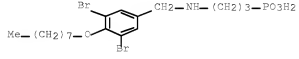


RN 569682-91-3 HCAPLUS
CN Phosphonic acid, [3-[[[3,5-dibromo-4-(octyloxy)phenyl]methyl]amino ]propyl]- (9CI) (CA INDEX NAME)



RN 569682-93-5 HCAPLUS
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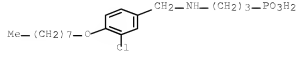
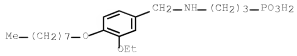
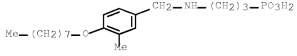


RN 569682-97-9 HCAPLUS

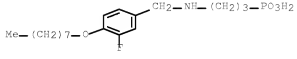
CN Phosphonic acid, [3-[[[3-ethoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



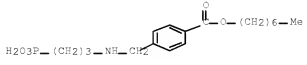
RN 569682-99-1 HCAPLUS
CN Phosphonic acid, [3-[[[3-methyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



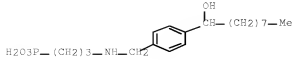
RN 569683-01-8 HCAPLUS
CN Phosphonic acid, [3-[[[3-fluoro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



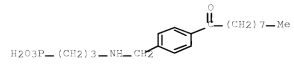
RN 569683-30-3 HCAPLUS
CN Benzoic acid, 4-[[(3-phosphonopropyl)amino]methyl]-, 1-heptyl ester (9CI) (CA INDEX NAME)



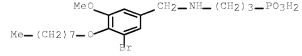
RN 569683-32-5 HCAPLUS
CN Phosphonic acid, [3-[[[4-(1-hydroxynonyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



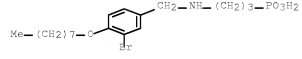
RN 569683-34-7 HCAPLUS
CN Phosphonic acid, [3-[[[4-(1-oxononyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



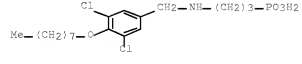
RN 569683-55-2 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-59-6 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-61-0 HCAPLUS
CN Phosphonic acid, [3-[[[3,5-dichloro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-63-2 HCAPLUS
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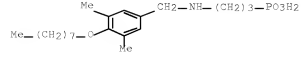
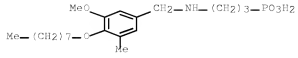
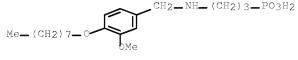


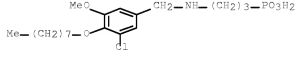
RN 569683-70-1 HCAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-5-methyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



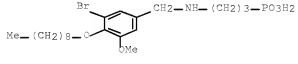
RN 569683-76-7 HCAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



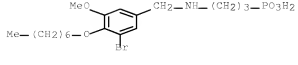
RN 569683-78-9 HCAPLUS
CN Phosphonic acid, [3-[[[3-chloro-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



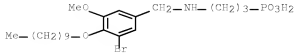
RN 569683-81-4 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(nonyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-82-5 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(heptyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-89-2 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(decyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-90-5 HCAPLUS
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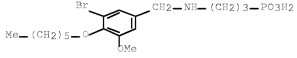
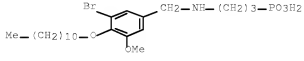
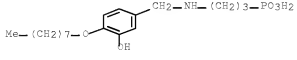


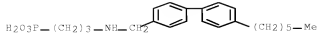
RN 569683-92-7 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(undecyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



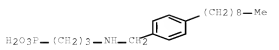
RN 569684-01-1 HCAPLUS
CN Phosphonic acid, [3-[[[3-hydroxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-32-8 HCAPLUS
CN Phosphonic acid, [3-[[(4'-hexyl[1,1'-biphenyl]-4-yl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-50-0 HCAPLUS
CN Phosphonic acid, [3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI)
(CA INDEX NAME)



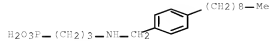

CC 1-3 (Pharmacology)
Section cross-reference(s): 25
IT 569682-67-3P 569682-68-4P 569682-73-1P
569682-91-3P 569682-93-5P 569682-97-9P
569682-99-1P 569683-01-8P 569683-30-3P
569683-32-5P 569683-34-7P 569683-55-2P
569683-59-6P 569683-61-0P 569683-63-2P
569683-70-1P 569683-76-7P 569683-78-9P
569683-81-4P 569683-82-5P 569683-89-2P
569683-90-5P 569683-92-7P 569684-01-1P
569684-32-8P 569684-50-0P 724458-96-2P
724458-97-3P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(selecting against S1P3 enhances acute cardiovascular tolerability of 3-(N-benzyl)aminopropylphosphonic acid S1P receptor agonists)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:465499 HCAPLUS Full-text
DOCUMENT NUMBER: 141:133550
TITLE: The discovery of 3-(N-alkyl)aminopropylphosphonic acids as potent S1P receptor agonists
AUTHOR(S): Hale, Jeffrey J.; Doherty, George; Toth, Leslie; Li, Zhen; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark; Milligan, James; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(13), 3495-3499
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:133550
ED Entered STN: 10 Jun 2004
AB 3-(N-Alkyl)aminopropylphosphonic acids are potent agonists of four of the five known sphingosine-1-phosphate (S1P) receptor subtypes and are useful in immunosuppressive therapy.
IT 569684-50-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation, immunomodulatory effect and structure-activity

relationship studies of 3-(N-alkyl)aminopropylphosphonic acids as potent S1P receptor agonists)

RN 569684-50-0 HCAPLUS

CN Phosphonic acid, [3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



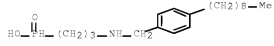
IT 569684-52-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation, immunomodulatory effect and structure-activity relationship studies of 3-(N-alkyl)aminopropylphosphonic acids as potent S1P receptor agonists)

RN 569684-52-2 HCAPLUS

CN Phosphinic acid, [3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)

Section cross-reference(s): 21

IT 569684-50-0P 725724-58-3P 725724-59-4P 725724-60-7P 725724-61-8P 725724-62-9P 725724-63-0P 725724-64-1P 725724-65-2P 725724-66-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation, immunomodulatory effect and structure-activity relationship studies of 3-(N-alkyl)aminopropylphosphonic acids as potent S1P receptor agonists)

IT 402615-91-2 569682-76-4 569682-79-7 569682-80-0 569682-84-4 569682-85-5 569682-86-6 569684-52-2 596819-84-0 597340-18-6 597340-90-4 597340-97-1 597341-03-2 597341-12-3 725724-57-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation, immunomodulatory effect and structure-activity relationship studies of 3-(N-alkyl)aminopropylphosphonic acids as potent S1P receptor agonists)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

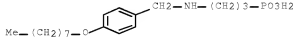
ACCESSION NUMBER: 2004:368306 HCAPLUS Full-text

DOCUMENT NUMBER: 141:99302

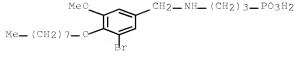
TITLE: Immune cell regulation and cardiovascular effects of sphingosine 1-phosphate receptor agonists in rodents are mediated via distinct receptor subtypes

AUTHOR(S): Forrest, M.; Sun, S.-Y.; Hajdu, R.; Bergstrom, J.; Card, D.; Doherty, G.; Hale, J.; Keohane, C.; Meyers, C.; Milligan, J.; Mills, S.;

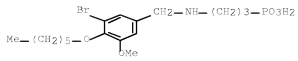
Nomura, N.; Rosen, H.; Rosenbach, M.; Shei, G.-J.; Singer, I. I.; Tian, M.; West, S.; White, V.; Xie, J.; Proia, R. L.; Mandala, S.
CORPORATE SOURCE: Departments of Immunology and Rheumatology, Pharmacology, and Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(2), 758-768
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 May 2004
AB Sphingosine 1-phosphate (S1P) is a bioactive lysolipid with pleiotropic functions mediated through a family of G protein-coupled receptors, S1P1,2,3,4,5. Physiol. effects of S1P receptor agonists include regulation of cardiovascular function and immunosuppression via redistribution of lymphocytes from blood to secondary lymphoid organs. The phosphorylated metabolite of the immunosuppressant agent FTY720 (2-amino-2-(2-[4- octylphenyl]ethyl)-1,3-propanediol) and other phosphonate analogs with differential receptor selectivity were investigated. No significant species differences in compound potency or rank order of activity on receptors cloned from human, murine, and rat sources were observed All synthetic analogs were high-affinity agonists on S1P1, with IC50 values for ligand binding between 0.3 and 14 nM. The correlation between S1P1 receptor activation and the ED50 for lymphocyte reduction was highly significant ($p < 0.001$) and lower for the other receptors. In contrast to S1P1-mediated effects on lymphocyte recirculation, three lines of evidence link S1P3 receptor activity with acute toxicity and cardiovascular regulation: compound potency on S1P3 correlated with toxicity and bradycardia; the shift in potency of phosphorylated-FTY720 for inducing lymphopenia vs. bradycardia and hypertension was consistent with affinity for S1P1 relative to S1P3; and toxicity, bradycardia, and hypertension were absent in S1P3-/- mice. Blood pressure effects of agonists in anesthetized rats were complex, whereas hypertension was the predominant effect in conscious rats and mice. Immunolocalization of S1P3 in rodent heart revealed abundant expression on myocytes and perivascular smooth muscle cells consistent with regulation of bradycardia and hypertension, whereas S1P1 expression was restricted to the vascular endothelium.
IT 569682-67-3 569683-55-2 569683-90-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(immune cell regulation and cardiovascular effects of sphingosine 1-phosphate receptor agonists in rodents are mediated via distinct receptor subtypes)
RN 569682-67-3 HCAPLUS
CN Phosphonic acid, [3-[[[4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)




RN 569683-55-2 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-90-5 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(hexyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)




CC 1-7 (Pharmacology)
IT 26993-30-6, Sphingosine 1 phosphate 402615-91-2
569682-67-3 569683-55-2 569683-90-5
719286-66-5 719286-67-6
RL: PAC (Pharmacological activity); BIOL (Biological study)
(immune cell regulation and cardiovascular effects of sphingosine 1-phosphate receptor agonists in rodents are mediated via distinct receptor subtypes)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FULL SEARCH HISTORY

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=> d his nofile

     (FILE 'HOME' ENTERED AT 09:32:45 ON 27 JUL 2007)

     FILE 'HCAPLUS' ENTERED AT 09:33:39 ON 27 JUL 2007
               E US20050070506/PN
L1             1 SEA ABB=ON  PLU=ON  US20050070506/PN
               D ALL
               SEL RN

     FILE 'REGISTRY' ENTERED AT 09:34:34 ON 27 JUL 2007
L2           424 SEA ABB=ON  PLU=ON  (100-83-4/BI OR 101385-93-7/BI OR
                 101500-22-5/BI OR 103057-44-9/BI OR 103680-62-2/BI OR
                 103680-71-3/BI OR 10521-91-2/BI OR 106-41-2/BI OR
                 107-13-1/BI OR 108898-23-3/BI OR 110943-74-3/BI OR
                 111-70-6/BI OR 111-86-4/BI OR 1203-68-5/BI OR 1204-60-0
                 /BI OR 121-32-4/BI OR 121-33-5/BI OR 121118-78-3/BI OR
                 123-08-0/BI OR 130592-02-8/BI OR 13138-33-5/BI OR
                 131888-48-7/BI OR 13214-66-9/BI OR 13477-53-7/BI OR
                 13631-21-5/BI OR 13880-74-5/BI OR 139-85-5/BI OR
                 143-16-8/BI OR 146936-34-7/BI OR 148547-19-7/BI OR
                 149104-89-2/BI OR 15174-69-3/BI OR 167279-18-7/BI OR
                 169806-13-7/BI OR 17012-21-4/BI OR 18278-34-7/BI OR
                 188846-99-3/BI OR 19463-48-0/BI OR 198959-37-4/BI OR
                 2052-07-5/BI OR 208108-76-3/BI OR 2113-57-7/BI OR
                 2233-18-3/BI OR 2314-36-5/BI OR 23703-22-2/BI OR
                 2374-05-2/BI OR 24076-33-3/BI OR 24083-12-3/BI OR
                 24083-13-4/BI OR 2420-16-8/BI OR 2439-54-5/BI OR
                 246847-91-6/BI OR 2495-35-4/BI OR 25006-17-1/BI OR
                 256488-46-7/BI OR 2973-76-4/BI OR 2973-77-5/BI OR
                 2973-78-6/BI OR 3111-37-3/BI OR 3132-99-8/BI OR
                 3261-62-9/BI OR 3300-51-4/BI OR 3453-33-6/BI OR
                 350-92-5/BI OR 35622-27-6/BI OR 36476-78-5/BI OR
                 3761-92-0/BI OR 38841-98-4/BI OR 3964-56-5/BI OR
                 401-95-6/BI OR 40499-83-0/BI OR 4282-40-0/BI OR
                 4282-42-2/BI OR 4282-44-4/BI OR 4815-96-7/BI OR
                 49763-67-9/BI OR 49763-69-1/BI OR 500191-05-9/BI OR
                 50262-46-9/BI OR 50773-56-3/BI OR 51572-88-4/BI OR
                 542-69-8/BI OR 54256-43-8/BI OR 5438-36-8/BI OR
                 54784-14-4/BI OR 54963-70-1/BI OR 556-18-3/BI OR
                 56-12-2/BI OR 56217-93-7/BI OR 56308-79-3/BI OR
                 56962-11-9/BI OR 569682-66-2/BI OR 569682-67-3/BI OR
                 569682-68-4/BI OR 569682-69-5/BI OR 569682-70-8/BI OR
                 569682-71-9/BI OR 569682-72-0/BI OR 569682-73-1/BI OR
                 569682-74-2/BI OR 569682-75-3/BI OR 569682-77-5/BI OR
                 569682-78-6/BI OR 569682-79-7/BI OR 569682-80-0/BI OR
                 569682-81-1/BI OR 569
L3            71 SEA ABB=ON  PLU=ON  L2 AND 1/NR AND 1/P AND 1/N
               D 1-3 STR RSD
L4           154 SEA ABB=ON  PLU=ON  L2 AND 1/P

     FILE 'HCAPLUS' ENTERED AT 09:39:18 ON 27 JUL 2007
L5        140355 SEA ABB=ON  PLU=ON  L2

     FILE 'REGISTRY' ENTERED AT 09:39:32 ON 27 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 09:42:04 ON 27 JUL 2007
               D SCAN L1

     FILE 'REGISTRY' ENTERED AT 09:42:05 ON 27 JUL 2007
L6            23 SEA ABB=ON  PLU=ON  L4 AND C4N/RF
               D SCAN
L7             0 SEA ABB=ON  PLU=ON  L6 AND C4S/RF
L8            36 SEA ABB=ON  PLU=ON  L2 AND C4S/RF
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                D SCAN
L9           67 SEA ABB=ON  PLU=ON  L2 AND C4N/RF
L10           7 SEA ABB=ON  PLU=ON  L8 AND L9
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 09:47:31 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 09:58:25 ON 27 JUL 2007
L11           7 SEA ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12           1 SEA ABB=ON  PLU=ON  L10 AND L11
                D SCAN
                D SCAN L12
                D SCAN L11
L13          43 SEA ABB=ON  PLU=ON  L2 AND 3/F
L14          36 SEA ABB=ON  PLU=ON  L13 AND L8
L15           7 SEA ABB=ON  PLU=ON  L13 AND L10
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 10:03:40 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 10:05:33 ON 27 JUL 2007
L16          12 SEA ABB=ON  PLU=ON  L2 AND C3N/RF
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 10:06:39 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 10:07:56 ON 27 JUL 2007
L17           6 SEA ABB=ON  PLU=ON  L16 AND L8
L18           1 SEA ABB=ON  PLU=ON  L16 AND L11

     FILE 'STNGUIDE' ENTERED AT 10:08:37 ON 27 JUL 2007
                D SCAN L18

     FILE 'REGISTRY' ENTERED AT 10:08:53 ON 27 JUL 2007
                D SCAN L17
                D SCAN L18

     FILE 'STNGUIDE' ENTERED AT 10:09:12 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 10:12:52 ON 27 JUL 2007
                D RSD
L19          40 SEA ABB=ON  PLU=ON  L9 AND C6/RF AND 2/NR
L20           9 SEA ABB=ON  PLU=ON  L19 AND 4/O
                D SCAN
L21           1 SEA ABB=ON  PLU=ON  L20 AND C22 H33 N O4/MF
L22           2 SEA ABB=ON  PLU=ON  L9 AND 1/F
                D SCAN
                D SCAN L12
L23           1 SEA ABB=ON  PLU=ON  L16 AND 2/NR AND 2/O
                D SCAN
L24          22 SEA ABB=ON  PLU=ON  L9 AND 2/NR AND 2-3/O AND C6/RF
L25          11 SEA ABB=ON  PLU=ON  L24 AND 2/O
                D SCAN
L26           2 SEA ABB=ON  PLU=ON  L25 AND 21/C
                D SCAN
L27           4 SEA ABB=ON  PLU=ON  L24 AND 20/C AND 3/O
                D SCAN
L28           6 SEA ABB=ON  PLU=ON  L2 AND 2/BR
                D SCAN
L29           3 SEA ABB=ON  PLU=ON  L28 AND 2/NR
                D SCAN
                D QUE
L30           6 SEA ABB=ON  PLU=ON  L9 AND 2/NR AND 5/O AND 1/P
                D SCAN
L31           6 SEA ABB=ON  PLU=ON  L15 AND 4/NR
L32           5 SEA ABB=ON  PLU=ON  L31 AND 3/O
                D SCAN
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L33          27 SEA ABB=ON  PLU=ON  L3 AND 4/O
L34          10 SEA ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
                D SCAN
L35           5 SEA ABB=ON  PLU=ON  L34 AND 20-30/C
                D SCAN
L36          92 SEA ABB=ON  PLU=ON  L2 AND 2/NR NOT ((L8 OR L9) OR 11)

L37          44 SEA ABB=ON  PLU=ON  L2 AND ?BIPHENYL?/CNS
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 10:53:32 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 10:57:53 ON 27 JUL 2007
L38          32 SEA ABB=ON  PLU=ON  L37 AND 20-100/C
L39           0 SEA ABB=ON  PLU=ON  L38 AND 1/S
                D QUE
L40           0 SEA ABB=ON  PLU=ON  L37 AND 1-5/S
                D SCAN L3
L41          68 SEA ABB=ON  PLU=ON  L3 AND C6/RF
L42          68 SEA ABB=ON  PLU=ON  L41 AND 12-50/C
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:12:32 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 11:18:09 ON 27 JUL 2007
L43         157 SEA ABB=ON  PLU=ON  L6 OR (L10 OR L11 OR L12 OR L13 OR
                L14 OR L15 OR L16 OR L17 OR L18) OR (L19 OR L20 OR L21
                OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
                L29 OR L30 OR L31 OR L32 OR L33) OR L35 OR L38
L44         199 SEA ABB=ON  PLU=ON  (L41 OR L42 OR L43)

     FILE 'HCAPLUS' ENTERED AT 11:20:11 ON 27 JUL 2007
L45         849 SEA ABB=ON  PLU=ON  L44
L46             QUE ABB=ON  PLU=ON  PHARMAC?/SC,SX
L47         483 SEA ABB=ON  PLU=ON  L45 AND L46
                D SCAN L1
L48             QUE ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
                MY<2003 OR REVIEW/DT
L49         270 SEA ABB=ON  PLU=ON  L47 AND L48
L50             QUE ABB=ON  PLU=ON  IMMUNOSUPPRES? OR IMMUNOREG? OR
                IMMUN?(A)(SUPPRESS? OR REG?)
L51           7 SEA ABB=ON  PLU=ON  L49 AND L50
                D SCAN
                E IMMUNOSUPPRESSIVES/CT
                E IMMUNOSUP/CT
L52             QUE ABB=ON  PLU=ON  IMMUNOSUPPRESSANTS+PFT,OLD,NT/CT
L53             QUE ABB=ON  PLU=ON  IMMUNOSUPPRESSION+PFT,OLD,NT/CT
                E AGONIS/CT
                E AGON/CT
L54           6 SEA ABB=ON  PLU=ON  L49 AND (L52 OR L53)
                D SCAN
                E ANTAGONISTS/CT
                E ANTAG/CT
                E ANTAGONISM/CT
                E E3+ALL
L55             QUE ABB=ON  PLU=ON  ANTAGONISM+PFT,OLD,NT/CT
L56           0 SEA ABB=ON  PLU=ON  L49 AND L55
L57             QUE ABB=ON  PLU=ON  AGON? OR ANTAG?
L58          79 SEA ABB=ON  PLU=ON  L49 AND L57
                D L***_L*** KWIC
                D 70-79 KWIC
L59             QUE ABB=ON  PLU=ON  EDG1(A)S1P?
L60          19 SEA ABB=ON  PLU=ON  EDG1(A)S1P?
                D 1-3 KWIC
L61           2 SEA ABB=ON  PLU=ON  L60 AND L49
                D 1-2 KWIC
L62             QUE ABB=ON  PLU=ON  F(W)Y
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L63           0 SEA ABB=ON  PLU=ON  L49 AND L62
                E EDG1 RECEPTOR/CT
                E EDG1 AGONIST/CT
                E FTY/CT
                E GTP/CT
                E E3+ALL
                E GTP/CT
L64             QUE ABB=ON  PLU=ON  GTP? OR FTP?
L65           0 SEA ABB=ON  PLU=ON  L49 AND L64
L66             QUE ABB=ON  PLU=ON  720
L67           0 SEA ABB=ON  PLU=ON  L49 AND L66
L68             QUE ABB=ON  PLU=ON  AUTOIMMUN?
L69          21 SEA ABB=ON  PLU=ON  L49 AND L68
                D 1-5 KWIC
L70             QUE ABB=ON  PLU=ON  "AUTOIMMUNE DISEASE"+PFT,OLD,NT/CT

L71          32 SEA ABB=ON  PLU=ON  L49 AND L70
                D SCAN L1
                E INFLAMMATION/CT
L72             QUE ABB=ON  PLU=ON  INFLAMMATION+PFT,OLD,NT/CT
L73          41 SEA ABB=ON  PLU=ON  L49 AND L72
                E INFECTION/CT
                E INFECTIONS/CT
L74             QUE ABB=ON  PLU=ON  INFECTION+PFT,OLD,NT/CT
L75          15 SEA ABB=ON  PLU=ON  L49 AND L74
L76             QUE ABB=ON  PLU=ON  AIDS+PFT,OLD,NT/CT
L77           7 SEA ABB=ON  PLU=ON  L49 AND L76
L78             QUE ABB=ON  PLU=ON  ASTHMA+PFT,OLD,NT/CT
L79          16 SEA ABB=ON  PLU=ON  L49 AND L78
                D L1 IT
L80             QUE ABB=ON  PLU=ON  "RESPIRATORY SYSTEM, DISEASE"+PFT,O
                LD,NT/CT
L81          29 SEA ABB=ON  PLU=ON  L49 AND L80
L82             QUE ABB=ON  PLU=ON  ARTHRITIS+PFT,OLD,NT/CT
L83          22 SEA ABB=ON  PLU=ON  L49 AND L82
                E MUSCULAR DYSTRO/CT
L84             QUE ABB=ON  PLU=ON  "MUSCULAR DYSTROPHY"+PFT,OLD,NT/CT

L85           3 SEA ABB=ON  PLU=ON  L49 AND L84
L86             QUE ABB=ON  PLU=ON  "SKIN, DISEASE"+PFT,OLD,NT/CT
L87          30 SEA ABB=ON  PLU=ON  L49 AND L86
                E DERMATITIS/CT
                E E3+ALL
L88             QUE ABB=ON  PLU=ON  DERMATITIS+PFT,OLD,NT/CT
L89          12 SEA ABB=ON  PLU=ON  L49 AND L88
L90          68 SEA ABB=ON  PLU=ON  L51 OR L61 OR L69 OR L71 AND L73
                OR L75 OR L77 OR L79 OR L81 OR L83 OR L85 OR L89 OR
                L87
L91          24 SEA ABB=ON  PLU=ON  L58 AND L90
L92           7 SEA ABB=ON  PLU=ON  L90 AND L50
L93           2 SEA ABB=ON  PLU=ON  L90 AND L60
L94             QUE ABB=ON  PLU=ON  NEOPLASM+PFT,OLD,NT/CT
L95          44 SEA ABB=ON  PLU=ON  L49 AND L94
L96          32 SEA ABB=ON  PLU=ON  L95 AND L90
                SAV L96 JEA176HCP/A
                DEL SEL
                SEL L96 HIT RN
                D SCAN
                DEL SEL
                SEL L1 AU
L97        1272 SEA ABB=ON  PLU=ON  ("DOHERTY, GEORGE A."/AU OR
                "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/AU OR
                "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR "MANDALA,
                SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR "ROSEN,
                HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98             QUE ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99          714 SEA ABB=ON  PLU=ON  L97 AND L48
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L100        228 SEA ABB=ON  PLU=ON  L99 AND L98
L101         26 SEA ABB=ON  PLU=ON  L100 AND L50
L102          1 SEA ABB=ON  PLU=ON  L1 AND L101
L103         28 SEA ABB=ON  PLU=ON  L96 NOT L101
                D SCAN

     FILE 'REGISTRY' ENTERED AT 12:08:47 ON 27 JUL 2007
L104          1 SEA ABB=ON  PLU=ON  3300-51-4/RN
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 12:10:46 ON 27 JUL 2007

     FILE 'REGISTRY' ENTERED AT 12:12:43 ON 27 JUL 2007
L105        179 SEA ABB=ON  PLU=ON  L44 AND 18-70/C

     FILE 'HCAPLUS' ENTERED AT 12:13:38 ON 27 JUL 2007
L106         15 SEA ABB=ON  PLU=ON  L105
L107          0 SEA ABB=ON  PLU=ON  L106 AND L103
                D SCAN L106
                D L106 1-15 CC
L108          3 SEA ABB=ON  PLU=ON  L106 AND L48
                D SCAN

     FILE 'REGISTRY' ENTERED AT 12:18:30 ON 27 JUL 2007
L109         20 SEA ABB=ON  PLU=ON  L44 NOT L105
                D SCAN
L110          1 SEA ABB=ON  PLU=ON  L109 AND  C14 H24 N O4 P/MF
L111          1 SEA ABB=ON  PLU=ON  L109 AND  C17 H29 BR N O5 P/MF
L112        181 SEA ABB=ON  PLU=ON  L105 OR L110 OR L111

     FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007
L113         15 SEA ABB=ON  PLU=ON  L112
L114         15 SEA ABB=ON  PLU=ON  L106 OR L113
L115          3 SEA ABB=ON  PLU=ON  L114 AND L48
L116          3 SEA ABB=ON  PLU=ON  L115 AND (L50 OR (L52 OR L53) OR
                L55 OR L57 OR L59 OR L70 OR L72 OR L74 OR L76 OR L78
                OR L80)
L117          3 SEA ABB=ON  PLU=ON  L116 AND (L82 OR L84 OR L86 OR L88
                OR L94)
                D SCAN
                SAV L117 JEA176HCPA/A
L118          3 SEA ABB=ON  PLU=ON  L117 NOT L103
L119          0 SEA ABB=ON  PLU=ON  L117 NOT L101
L120          4 SEA ABB=ON  PLU=ON  L96 AND L50
                D SCAN
L121          0 SEA ABB=ON  PLU=ON  L120 NOT L101
                D QUE L101
L122         12 SEA ABB=ON  PLU=ON  L113 NOT (L118 OR L120)
                D SCAN
                SAV L122 JEA176HCPB/A

     FILE 'REGISTRY' ENTERED AT 12:39:55 ON 27 JUL 2007
L123          0 SEA ABB=ON  PLU=ON  L112 AND MEDLINE/LC
L124          0 SEA ABB=ON  PLU=ON  L112 AND BIOSIS/LC
L125          0 SEA ABB=ON  PLU=ON  L112 AND DRUGU/LC
L126          0 SEA ABB=ON  PLU=ON  L112 AND EMBASE/LC
                D QUE

     FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 12:40:59 ON 27
     JUL 2007
L127          0 SEA ABB=ON  PLU=ON  L126
L128        608 SEA ABB=ON  PLU=ON  L97
L129        277 SEA ABB=ON  PLU=ON  L128 AND L98
L130        143 SEA ABB=ON  PLU=ON  L129 AND L48
L131          6 SEA ABB=ON  PLU=ON  L130 AND (L50 OR L59)
                D 1-6 TI
                SAV L131 JEA176MULTIN/A
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     FILE 'STNGUIDE' ENTERED AT 12:44:10 ON 27 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 12:45:23 ON 27 JUL 2007
                SAV L101 JEA176HCPIN/A

     FILE 'STNGUIDE' ENTERED AT 12:46:17 ON 27 JUL 2007
                D QUE L101
                D QUE L101
                D QUE L131

     FILE 'HCAPLUS, MEDLINE, BIOSIS' ENTERED AT 12:49:36 ON 27 JUL 2007
L132          29 DUP REM L101 L131 (3 DUPLICATES REMOVED)
                     ANSWERS '1-26' FROM FILE HCAPLUS
                     ANSWERS '27-29' FROM FILE BIOSIS
                D L132 1-29 IBIB ED AB
L133           4 SEA ABB=ON  PLU=ON  (L106 OR L96) AND L101
                D SCAN
                D QUE L133
                D L133 1-4 IBIB ED ABS FHITSTR HITIND

     FILE 'STNGUIDE' ENTERED AT 13:04:20 ON 27 JUL 2007
                D QUE L119
                D QUE L121
                D QUE L122
                D QUE L127

     FILE 'HCAPLUS' ENTERED AT 13:06:51 ON 27 JUL 2007
L134          12 DUP REM L119 L121 L122 L127 (0 DUPLICATES REMOVED)
                     ANSWERS '1-12' FROM FILE HCAPLUS
                D L134 1-12 IBIB ED ABS HITSTR HITIND
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